# **ORIGINAL RESEARCH**

# Effect of Religious Fasting in Ramadan on Blood Pressure: Results From LORANS (London Ramadan Study) and a Meta-Analysis

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**BACKGROUND:** Ramadan fasting is practiced by hundreds of millions every year. This ritual practice changes diet and lifestyle dramatically; thus, the effect of Ramadan fasting on blood pressure must be determined.

**METHODS AND RESULTS:** LORANS (London Ramadan Study) is an observational study, systematic review, and meta-analysis. In LORANS, we measured systolic blood pressure (SBP) and diastolic blood pressure (DBP) of 85 participants before and right after Ramadan. In the systematic review, studies were retrieved from PubMed, Embase, and Scopus from inception to March 3, 2020. We meta-analyzed the effect from these studies and unpublished data from LORANS. We included observational studies that measured SBP and/or DBP before Ramadan and during the last 2 weeks of Ramadan or the first 2 weeks of the month after. Data appraisal and extraction were conducted by at least 2 reviewers in parallel. We pooled SBP and DBP using a random-effects model. The systematic review is registered with PROSPERO (International Prospective Register of Systematic Reviews; CRD42019159477). In LORANS, 85 participants were recruited; mean age was  $45.6\pm15.9$  years, and 52.9% (n=45) of participants were men. SBP and DBP after Ramadan fasting were lower by 7.29 mm Hg (-4.74 to -9.84) and 3.42 mm Hg (-1.73 to -5.09), even after adjustment for potential confounders. We identified 2778 studies of which 33 with 3213 participants were included. SBP and DBP after/before Ramadan were lower by 3.19 mm Hg (-4.43 to -1.96,  $l^2=48\%$ ) and 2.26 mm Hg (-3.19 to -1.34,  $l^2=66\%$ ), respectively. In subgroup analyses, lower blood pressures were observed in the groups who are healthy or have hypertension or diabetes but not in patients with chronic kidney disease.

**CONCLUSIONS:** Our study suggests beneficial effects of Ramadan fasting on blood pressure independent of changes in weight, total body water, and fat mass and supports recommendations for some governmental guidelines that describe Ramadan fasting as a safe religious practice with respect to blood pressure.

Key Words: diastolic blood pressure 
hypertension 
meta-analysis 
Ramadan fasting 
systematic review 
systolic blood pressure

Ramadan is the ninth month of the Islamic calendar and lasts 29 or 30 days based on the visibility of the crescent moon. Fasting in this month is 1 of the 5 pillars of Islam and Muslims observe it every year. Ramadan fasting is classified as a model of intermittent fasting.<sup>1</sup> However, the conventional models

of intermittent fasting allow drinking noncaloric beverages (ie, water, tea, and black coffee) during fasting periods.<sup>2</sup> In Ramadan, however, Muslims abstain from eating, drinking, smoking, sexual intercourse, and medication during daylight hours.<sup>3</sup> Usually, Muslims have 2 basic meals during Ramadan, one is predawn

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# **CLINICAL PERSPECTIVE**

## What Is New?

 Ramadan fasting is associated with a reduction of systolic blood pressure and diastolic blood pressure in individuals who are healthy or have hypertension or diabetes (this effect is independent of weight and total body water reduction).

## What Are the Clinical Implications?

 This study provides updated evidence-based information for clinicians and policy makers that Ramadan fasting may have beneficial effects on blood pressure.

## Nonstandard Abbreviations and Acronyms

LORANS London Ramadan Study

(Suhur), and the other is after sunset (Iftar). This dietary change is the key change in their lifestyle; however, the changes are not limited to that and lifestyles may be modified dramatically during this month. This lifestyle modification could have acute as well as longterm consequences for health. Although hundreds of millions of Muslims practice Ramadan fasting worldwide, the effect of this ritual on health is not adequately studied. Blood pressure could be acutely affected by such changes in dietary intake and timing, physical activity, and sleep patterns including among individuals with hypertension. Studies on the effect of Ramadan fasting on blood pressure, however, are inconclusive. Although several studies have shown reductions in systolic (SBP) and diastolic blood pressure (DBP),4-8 others have reported an increase<sup>9,10</sup> or no changes in blood pressure.<sup>11–15</sup> The available studies are limited in number and sample size and suffer from suboptimal sampling methods. For instance, many of the previous studies recruited samples such as students,<sup>9</sup> workers,<sup>6</sup> and patients with chronic disease who have regular visits to clinics,<sup>4</sup> which may not represent the whole community. Therefore, we conducted the LORANS (London Ramadan Study) in which we collected data from participants in London to assess the effect of Ramadan fasting on blood pressure using a comprehensive data analysis. We recruited a multicultural community-based sample and measured SBP and DBP pressure before and after Ramadan.

So far, 6 systematic reviews assessed the effect of Ramadan fasting on blood pressure.<sup>16–21</sup> They are either outdated (2013) or not comprehensive. Two of these reviews performed a meta-analysis; however, one was

only on patients with chronic kidney disease (CKD),<sup>18</sup> and the other was on healthy individuals and did not pool DBP.<sup>19</sup> Because of the inconsistency in prior studies, we undertook a systematic review and meta-analysis on the effect of Ramadan fasting on blood pressure.

## **METHODS**

The data that support the findings of this study are available from the corresponding author upon reasonable request.

## London Ramadan Study

LORANS is a longitudinal study that recruited individuals who were fasting in Ramadan 2019 in London.<sup>22</sup> We initially contacted 6 large mosques to be recruitment locations; 1 of the 6 mosques was unable to provide us with an agreement letter on time (before applications submission deadline to seek ethical approval), so it was not involved in the study. We invited people to participate via banners and flyers in the 5 mosques in London (2 in North West London, 1 in East London, 1 in Central London, and 1 in South London). We launched a website for the study to enable potential participants to know more about it and book appointments. Inclusion criteria were being over 18 years old and planning to fast ≥20 days of Ramadan. Exclusion criteria were pregnancy and not being available for the second visit after Ramadan. We set up a clinic for sampling in each of the 5 mosques. We enrolled 146 individuals who attended the pre-Ramadan visit, of whom 85 (58.2%) participants attended the second visit (during the second week after Ramadan). Table S1 compares characteristics of LORANS participants (n=85) to those of individuals who attended the first visit only (n=61); those not attending were younger age and none of them was a daily smoker. The main reasons for not attending the second visit were traveling and missing contact details (Figure S1). The study was conducted in Spring (April 25-June 16, 2019), and the fasting duration was 15.5 hours/day.

A review on methods of measuring blood pressure reported that the best scenario for measuring blood pressure should be 2 or 3 measurements with an interval between consecutive readings between 30 and 60 seconds.<sup>23</sup> Therefore, we measured blood pressure using an automatic blood pressure monitor (Omron 705-IT) 3 times with 30-second intervals while participants were sitting before blood extraction and calculated the average of the 3 measurements. We also measured height using a stadiometer (Leicester Height Measure) and weight (Marsden digital weighing scale) without heavy outer clothes or shoes; we measured waist circumference (just above the hip bones) and hip circumference (at widest part) using a tape measure with participant standing and took the average of 2 measures at each visit (participants were not fasting at both visits). Fat percentage, fat mass, fat-free mass, and total body water (TBW) were measured by a bioelectrical impedance analyser (Tanita BC-418) as well as fat percentage, fat mass, fat-free mass, and predicted muscle for each limb. Participants filled out questionnaires about their lifestyle, socioeconomic and demographic data, health status and medical history, and a 3-day food diary before Ramadan and during Ramadan to assess change in diet.

All participants provided informed consent. The study is ethically approved by the Imperial College Research Ethics Committee (reference: 19IC5138, dated April 17, 2019).

### **Systematic Review**

We followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses guidelines in structuring this systematic review (Table S2). We registered the study protocol with PROSPERO (International Prospective Register of Systematic Reviews; CRD42019159477).

#### **Eligibility Criteria**

We aimed to include published and unpublished studies that measured SBP and/or DBP twice. The first measurement had to be before Ramadan and the second measurement either during the last 2 weeks of Ramadan or the first 2 weeks of the month after (Shawaal). Also, means and SDs of SBP and DBP were needed. We excluded review articles, studies that introduced interventions (eg, exercise), and abstracts not associated with full texts.

#### Information Sources, Search, and Study Selection

We searched PubMed, Scopus, and Embase to locate all related published studies in all languages from inception until March 3, 2020. We used the following search terms "(Ramadhan OR Ramazan OR Ramadan OR (Islam\* AND fast\*)) AND (diastolic OR systolic OR hypertens\* OR blood pressure OR cardiovasc\* OR health)." We also contacted authors of related conference abstracts retrieved from the electronic databases to check if they had a full text.

Titles and abstracts of all retrieved studies were screened. At the next phase, full texts of eligible studies were evaluated against the inclusion/exclusion criteria to identify the final included studies. All these steps were conducted independently by at least 2 reviewers (R. A., S. A., S. Z.) in parallel; any disagreement was adjudicated by consensus.

#### **Data Collection Process**

At least 2 independent authors (R. A., V. L., M. Z. T.) used a data extraction master sheet to extract the following

information from the included articles: authors(s), year, journal, country, ethnicity, study site, type of blood pressure monitor, number and time of visits for measurements, number of subjects, age, population characteristics, duration of daytime (hours of fasting), and SBP and DBP measurements. Disagreements were resolved by consensus.

## **Risk of Bias**

We adapted the Newcastle-Ottawa Quality Assessment Scale for cohort studies<sup>24</sup> to evaluate the quality of selected studies in this review. Given that the selected studies in our review are not cohort studies, we needed to reframe questions on exposed and nonexposed subjects with maintaining the aim of these questions. Also, based on the characteristics of selected studies, we decided on which answers should contribute to a higher evaluation (eg, studies that recruited >100 participants were considered large studies).

The scale (Data S1) covers 3 areas: selection, comparability, and outcome assessment. Studies with a quality score of 4 or less are considered low quality, a quality score of 5 to 6 is considered satisfactory, a quality score of 7 to 8 is considered good, and a quality score of 9 to 10 is considered very good. This rating process was undertaken by at least 2 independent reviewers (R. A., V. L., M. Z.) in parallel and any disagreement was adjudicated by consensus; more details are provided in Table S3.

# Estimation of Daytime Temperature and Duration of Fasting Per Day

We used the Islamic Finder website to match the Islamic calendar to the Gregorian calendar to know when Ramadan started in different years.<sup>25</sup> Moreover, using the same site, we assessed the duration of fasting per day by calculating the average of the period between the sunrise prayer (Fajr) and sunset prayer (Maghrib) in the first day and that of the last day of Ramadan. Furthermore, to estimate daytime temperature to which participants of a particular study were exposed, we used a website that has records of past weather conditions back to September 2009 (no weather data available for older studies).<sup>26</sup> We used the highest temperature during the month of Ramadan as a proxy for daytime temperature in 29 studies (Table S4).

### Statistical Analysis London Ramadan Study

We used a linear mixed-effects model in the "Ime4" package (version 1.1-21) in R to investigate the effect of Ramadan fasting on SBP and DBP accounting for potential confounders. We added potential confounders to the model either as fixed or random effect variables. Fixed variables are those we need to observe their

effect on the model: age, sex, smoking status, weight, TBW, and fat mass. Random variables are those we need to ensure that they do not introduce random effects on the model: site of data collection and time gap between end of Ramadan and the second measurement. We constructed 4 models, adjusting for (1) age, sex, site, and time gap between end of Ramadan and the second measurement; (2) further adjusted for smoking status; (3) further adjusted for weight; and (4) adjusted for the variables in (2) plus TBW and fat mass. Weight was not added to the fourth model owing to potential collinearity. Furthermore, Table S5 shows further adjustments for sleep duration and energy intake.

Because of the limited number of predictive variables, we have followed a complete case analysis strategy. SBP and DBP before and after Ramadan are presented as mean $\pm$ SD; results of the mixed-effects models are reported in the form of a mean difference and 95% Cl. *P* value of <0.05 is considered statistically significant.

#### Meta-Analysis, Metaregression, and Sensitivity Analysis

We used "meta" package (version 4.11-0) in R to perform the meta-analysis and metaregression. We used the difference in means and 95% Cls to estimate the effect of Ramadan fasting on SBP and DBP, and a *P* value of <0.05 was considered statistically significant. We assessed between-study heterogeneity using  $I^2$  and pooled outcomes using an inverse variance weighted random-effects model. We conducted subgroup analyses among healthy individuals, patients with diabetes (type 2), patients with hypertension, and patients with CKD based only on 3 studies or more.

We used the "meta" package to conduct univariate metaregression to investigate associations of potential effect modifiers (temperature during Ramadan, duration of daily fasting, mean age, and dropout rate) and the effect of Ramadan fasting on the mean differences of SBP and DBP. We report results of metaregression in the form of  $\beta$ -coefficient and *P* value.

To assess the risk of small-study effects bias across studies, we checked the funnel plots and performed Egger's regression asymmetry test. If the Egger's test P value was <0.1 and/or the plot was considered asymmetric, we used the trim and fill method to correct for asymmetry and estimated the effect while adjusting for small-study effects bias.

All data were analyzed in R for Windows 3.6.1.

## RESULTS

#### London Ramadan Study

Baseline characteristics of LORANS' participants are shown in Table 1. Mean age was  $45.6\pm15.9$  years, with

#### Table 1. Sociodemographic and Lifestyle Status of LORANS' Participants (n=85)

Variable	Subgroups	Value
Age, y, mean±SD	Total	45.6±15.9
	18–40 (%)	31.8%
	40-60 (%)	49.4%
	60-80 (%)	17.6%
	>80 (%)	1.2%
Sex (male %)	52.9%	
Ethnic background, %	Pakistani	16.5%
	Indian	26.6%
	Bangladeshi	8.9%
	Somali	16.5%
	Arab	16.5%
	Other	15.2%
Marital status, %	Single	22.8%
	Married/living with a partner	73.4%
	Divorced/separated	3.8%
With chronic diseases, %	Diabetes	14%
	Hypertension	24%
	Cardiovascular diseases	5.2%
Education, %	No formal qualification	12.7%
	Secondary school or equivalent	25.3%
	Higher education: College/Higher National Certificate/ Higher National Diploma	21.5%
	Vocational qualification	1.3%
	Bachelor's degree	26.6%
	Postgraduate degree	12.7%
Smoking, %	Never	77.6%
	Stopped	14.1%
	Occasionally	3.5%
	Yes, most or all days	4.7%

LORANS indicates London Ramadan Study.

52.9% (n=45) men. Using the base model, SBP and DBP were lower after Ramadan fasting by 7.29 mm Hg (-4.74 to -9.84) and 3.42 mm Hg (-1.73 to -5.09), respectively, with findings robust to adjustments for potential confounding variables (Table 2, Figures S2 and S3).

### Systematic Review Search Results

We screened a total of 2778 titles/abstracts and removed 831 duplicates and excluded 1895 studies as ineligible, leaving 52 full texts of potential studies. We

	Before	After	Mean difference (95% (	CI)		
	Ramadan (mean±SD)	Ramadan (mean±SD)	Base model	Second model	Third model	Fourth model
Systolic blood pressure	132.2±20.1	124.9±17.5	-7.29 (-4.74 to -9.84)*	-7.29 (-4.74 to -9.84)*	-7.22 (-4.67 to -9.85)*	-7.34 (-4.63 to -10.10)*
Diastolic blood pressure	77.4±9.7	74±9.2	-3.42 (-1.73 to -5.09)*	-3.42 (-1.73 to -5.09)*	-3.17 (-1.48 to -4.87)*	-3.00 (-1.19 to -4.83)*

Table 2.	Systolic Blood Pressure and Diastolic Blood Pressure Before and After Ramadan Fasting and the Mean
Differen	ce Using Different Mixed-Effects Models in LORANS

Base model adjusts for age, sex, site, and second measurement day. Second model adjusts for base model variables and smoking status. Third model adjusts for second model variables, total body water, and fat mass. LORANS indicates London Ramadan Study.

\*P<0.001.

excluded 17 studies that involved interventions besides Ramadan fasting (eg, exercise programs), 11 studies judged to be low quality (with a high risk of bias; average quality score=3.9), and 7 further studies that included patients with specific conditions (eg, transplant kidney recipients). That left 33 studies (including LORANS) for the meta-analysis with a total of 3213 individuals (Figure 1).

#### **Study Characteristics**

The characteristics of the included studies are displayed in Table 3. Out of the 33 studies, 7 (13.2%; 423 of the participants) were done in Iran, 3 (4.5%; 144) in Pakistan, and 3 (3.5%; 113) in Turkey. Included studies targeted 4 groups of individuals: healthy individuals (23.3%; 749), patients with type 2 diabetes (55.5%; 1783), patients with hypertension (3.5%; 114), and those with CKD (19.1%; 614). The included studies measured blood pressure by different devices (Table 3); only 2 of them used 24-hour ambulatory blood pressure monitoring.<sup>27,28</sup> Table S3 shows the quality assessment and risk of bias in all potential studies. Eight of the included studies had high quality with low risk of bias (good), and 24 were moderate quality with moderate bias (moderate).

#### Effect on Blood Pressure

Most studies showed lower SBP and DBP in the last 2 weeks of Ramadan or the first 2 weeks of Shawaal. Across all studies, SBP was lower by 3.19 mm Hg (95% Cl, -4.43 to -1.96,  $l^2=48\%$ ) (Figure 2) and DBP by 2.26 mm Hg (95% Cl, -3.19 to -1.34,  $l^2=66\%$ ) (Figure 3).

#### **Subgroup Analyses**

Only 4 groups had a sufficient number (3 or more) of relevant studies for meta-analysis: healthy individual s,<sup>5,6,13,26,29–36,51,52</sup> patients with hypertension,<sup>26,27,37,38</sup> patients with diabetes,<sup>4,10,38–44</sup> and patients with CKD.<sup>45–50,53</sup> Studies that included different types of participants were divided into subsets and each subset was added as an independent study to the relevant

group. LORANS has 3 subsets (healthy, diabetes, and hypertension), Al-Nasir and Niazi's study<sup>38</sup> has 2 subsets (diabetes and hypertension), and Norouzy et al's study<sup>27</sup> has 2 subsets (healthy and hypertension). Conducting meta-analysis on the 4 groups of study participants yielded different pooled effect estimates of Ramadan fasting on blood pressure.

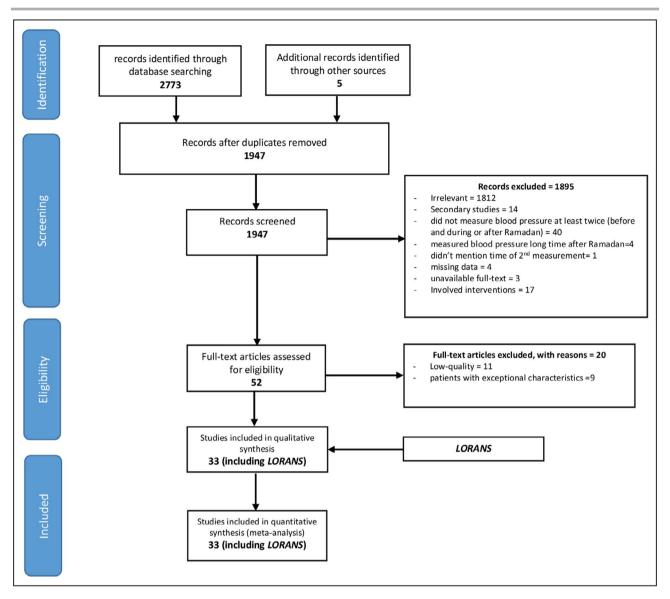
Subgroup analysis shows that Ramadan fasting was associated with lower BP among healthy individuals: SBP –3.21 mm Hg (–4.79 to –1.64,  $l^2$ =44%) and DBP –2.82 mm Hg (–4.34 to –1.30,  $l^2$ =70%); ndividuals with hypertension: SBP –8.44 mm Hg (–15.16 to –1.72,  $l^2$ =0%) and DBP –4.52 mm Hg (–7.75 to –1.28,  $l^2$ =24%); and individuals with diabetes: SBP –3.53 mm Hg (–6.14 to –0.93,  $l^2$ =61%) and DBP –2.13 mm Hg (–3.59 to –0.67,  $l^2$ =61%). There was no difference in patients with CKD (Figures 2 and 3).

#### **Small-Study Effects Bias**

Funnel plots did not indicate any asymmetry in the overall analysis. Also, the Egger's test showed no bias. However, there was an indication of bias from funnel plots and Egger's test *P* value in 2 of the 4 subgroups (Figure S4). We used the trim and fill method to correct for asymmetry among the subgroup of individuals with diabetes for DBP (Egger's test *P*=0.05), and the subgroup of patients with CKD for SBP (Egger's test *P*=0.07) and DBP (Egger's test *P*=0.05). The magnitude and the direction of effect were the same in these subgroups before and after using the trim and fill method (Table S6).

#### **Metaregression**

Daytime temperature during Ramadan was associated with a larger mean difference in SBP ( $\beta$ =0.34 mm Hg/°C, 0.06–0.63) and DBP ( $\beta$ =0.19 mm Hg/°C, 0.05–0.33) before-after Ramadan (Figures S5 and S6). There was no association between the duration of fasting per day and the mean difference in SBP or DBP (Figures S7 and S8). Similarly, there was no association between mean age or dropout rate and the changes in SBP and DBP (Figures S9 through S12).



**Figure 1.** Flow chart of studies included in this systematic review. LORANS indicates London Ramadan Study.

## DISCUSSION

LORANS showed that Ramadan fasting is associated with reduced SBP and DBP independently of weight, TBW, and fat mass. Similarly, our meta-analysis of 33 studies with 3213 participants including LORANS, found that Ramadan fasting was associated with lower SBP and DBP. However, subgroups analysis showed that this reduction is absent in patients with CKD.

So far, 6 systematic reviews investigated the effect of Ramadan fasting on blood pressure. The previous 6 systematic reviews included 44 studies that were considered and evaluated against our inclusion criteria in this review. Out of these studies, 18 studies were included: 8 were excluded owing to low quality.<sup>9,12,54–59</sup> and 4 were excluded because BP was measured more than 2 weeks after Ramadan.  $^{\rm 60-63}$ 

# Agreement With Studies of Intermittent Fasting

Although there are differences between Ramadan fasting and the common types of intermittent fasting, our findings are consistent with results of previous studies on intermittent fasting. Two studies reported that alternate day fasting is associated with lower SBP and DBP.<sup>64,65</sup> Also, another randomized trial that allocated participants to 2 fasting groups (intermittent energy restriction and continuous energy restriction) showed the same effects on SBP and DBP in both groups.<sup>66</sup>

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Author(s) and year	Country	L	Age, y	Men (%)	Dropout %	BP device	SBP before Ramadan	SBP right after Ramadan	Effect on SBP	DBP before Ramadan	DBP right after Ramadan	Effect on DBP
Ongsara et al (2017) <sup>31</sup>	Thailand	65	MN	MN	9	Automatic monitor	113.5±16.9	113.7±17.6	<i>←</i>	73±13.6	72.3±12.4	
Dewanti et al (2006) <sup>6</sup>	Indonesia	75	39±10	100	19.4	MM	129.4±29.7	120.5±25.5	→	84.5±14.3	75±10.3	→
Khan et al (2017) <sup>29</sup>	Pakistan	35	21.7±0.7	51.4	0	MN	113.1±10.5	113.6±9.5	←	74.7±7.1	75.9±6.9	←
Faris et al (2012) <sup>51</sup>	Jordan	50	MN	42	WN	Mercury sphygmomanometer	112.3±10	104.4±9	→	76.2±8.5	71.6±10.4	→
Malekmakan et al (2017) <sup>52</sup>	Iran	93	37.2±7.9	52.7	ΨZ	Aneroid sphygmomanometer	101.7±12.9	99.4±12.7	→	72.3±4.9	70.9±5.3	→
Gupta et al (2013) <sup>13</sup>	India	98	MM	100	0	M	121.9±10.5	121.2±8.9	→	76.9±7.6	76.65±6.7	
Shehab et al (2012) $^{\infty}$	UAE	60	MN	ъ Z	36.3	Mercury sphygmomanometer	122.2±19.1	118.6±17.8	→	75.3±14.1	75.3±14.1	:
Norouzy et al (2017) <sup>27</sup>	Iran	12	56.4±6.8	44.4	MN	24 h BP monitor	119.5±6	117.6±9	→	78.5±8	77.7±10	→
Sijavandi et al (2015) <sup>33</sup>	Iran	89	35±NM	57.3	11	Digital sphygmomanometer	116.4±11.1	115.5±10.1	→	80.5±5.6	79.3±8.2	→
Beltaifa et al (2002) <sup>30</sup>	Tunisia	20	43±14	60	MN	MN	110±10	110±10	:	70±10	65±5	
Martin et al (2004) <sup>34</sup>	Spain	17	MN	100	0	MM	108.5±8.3	102.9±10.5	→	68.8±9.8	60.9±6.4	→
Alsubheen et al (2017) <sup>35</sup>	Canada	o	32.3±7.8	100	0	Sphygmomanometer	120±11	109±12	→	77±7	71±7	→
Mohammadzade et al (2017) <sup>36</sup>	Iran	30	29.4±7.4	100	ΣZ	WN	124.7±4	121.6±6	→	80.3±8	79.2±8	→
Dasgupta (2017) <sup>5</sup>	Bengal	34	32.2±10.5	41.2	21	MM	114.9±15.3	107.8±15.4	→	74.2±9.6	69.1±8.9	→
Salahddin et al (2014) $^{37}$	India	15	44.6±5.6	MN	MN	Automatic monitor	148±19.6	132.5±17.9	→	90.4±7.8	81.1±6.3	→
Perk et al $(2001)^{28}$	NM	17	56.6±6.9	88.2	NM	24 h BP monitor	138.5±18.5	136.4±20.4	→	77.2±8.1	75.7±5.9	→
Al-Nasir & Niazi (1996) <sup>38</sup>	MN	28	NM	42.9	0	Mercury sphygmomanometer	146.5±24.9	140.7±28.6	→	81.5±9.3	77.9±9.6	→
Gholami et al (2018) <sup>39</sup>	Iran	54	NM	MN	10	MM	122.4±16.2	117.9±21.4	Ļ	80.2±13.3	79.8±13.7	→
Shao et al (2018) <sup>40</sup>	Singapore	62	52.2±11.1	54.4	MN	MM	140.1±19.1	130.9±2	→	80.5±9.6	76.9±7.4	→
Sahin et al (2013) <sup>41</sup>	NM	88	56.9±9.6	32.8	NM	MM	140±20.9	140±20	:	81.5±12.7	79.6±10.2	→
Norouzy et al (2012) <sup>42</sup>	Iran	88	51.3±10.6	51.1	15	Automatic monitor	130±15	129±15	→	77±10	79±11	<b>↓</b>
Khan et al (2012) <sup>43</sup>	Pakistan	75	52.8±8.5	50.6	58.1	MM	124.3±17.4	119.9±12.5	→	82.2±8.8	79.3±9.2	→
Bener & Yousafzai (2014) <sup>4</sup>	Qatar	1301	45.9±15.3	51.9	0	Mercury sphygmomanometer	130.6±14.3	125.8±14.2	→	81.4±9.3	77.6±8.9	→
Yarahmadi et al (2003) <sup>44</sup>	Iran	57	NM	MN	MM	MM	124.5±26.4	119.9±22	→	82.2±12.8	78.2±11.7	→
Traore et al (2014) <sup>10</sup>	Mali	25	48.5±6.8	56	31	Sphygmomanometer	123±12	136±21	←	83±10	86±9	←
Imtiaz et al (2016) <sup>45</sup>	Pakistan	34	47.7±14.6	64.7	MN	MZ	143.5±21	141.4±22.5	→	83.3±13.2	79.4±10.9	→

(Continued)

Author(s) and year	Country	2	Age, y	Men (%)	Dropout %	BP device	SBP before Ramadan	SBP right after Ramadan	Effect on SBP	DBP before Ramadan	DBP right after Ramadan	Effect on DBP
Alshamsi et al (2016) <sup>46</sup>	Saudi Arabia	407	53.3±16.2	52	× Z	WN	141.7±23.9	143.2±23.9	÷	73.1±15.3	75.1±16.4	<i>←</i>
Wan et al (2014) <sup>47</sup>	Malaysia	35	MZ	MN	MN	MN	148±19	149±17	←	78±9	79±9	←
Al-Wakeel (2014) <sup>48</sup>	Saudi Arabia	39	52.1±18.3	23	MN	MM	133.7±18.4	133.9±21.4	Ļ	76.9±14	76.2±14.3	→
Bernieh et al (2010) <sup>49</sup>	UAE	31	MN	MN	31.1	NM	138±13.2	131±26.3	$\rightarrow$	81.3±9	80±10	→
Kara et al (2017) <sup>50</sup>	Turkey	45	66.8±10.3	68.8	MN	MN	147.5±27.5	146.8±28.1	$\rightarrow$	87±14.5	86.4±14.4	→
Ekinic et al (2018) <sup>53</sup>	Turkey	23	45.6±10.6	16.1	4.2	Automatic monitor	131.5±16.5	127.7±14.8	$\rightarrow$	74.5±6.3	73.1±5.8	→
LORANS (2019)	UK	85	45.4±16	52.9	41.4	Automatic monitor	130.7±23	124.9±17.5	$\rightarrow$	77.4±9.7	74±9.2	→
BP indicates blood pressure; LORANS London Ramadan Study; NM, I	sure; LORANS	S Londor	n Ramadan Stu	dy; NM, not	mentioned; and	not mentioned; and SBP, systolic blood pressure.	sure.					

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# Effects of Weight Loss and Underlying Mechanisms

Lower blood pressure with fasting has been attributed to the metabolic switch (in which the body switches to use ketones for energy instead of glucose after 8-12 hours of fasting) in a recent review on intermittent fasting.67 Insulin drop during the metabolic switch is suggested to be the key reason behind reduced blood pressure after fasting.<sup>67–71</sup> Blood pressure is inversely correlated with parasympathetic nervous system activity and correlated with sympathetic nervous system activity; when the sympathetic nervous system activity is triggered by insulin, adrenal glands produce norepinephrine, which binds to a-receptors in the blood vessels; consequently, vasoconstriction occurs.71-74 Also, insulin acts downstream and enhances renal tubular sodium reabsorption, which confers more water retained in the circulation; as a result, blood pressure is raised.68,71 Other human and animal studies associate this reduction to the release of brain-derived neurotrophic factor, which elevates parasympathetic nervous system activity and improves insulin sensitivity.69,72,75 This mechanism may explain the increase in SBP in 1 of the included studies,<sup>10</sup> because the authors reported that 6 participants out of the 25 (24%) stopped their antidiabetic medications during Ramadan. Also, 3 participants (12%) in the same study stopped their antihypertensive medication, and only 4 participants (16%) visited their general practitioners during Ramadan.

On the other hand, Faris et al argued that blood pressure changes during and after Ramadan fasting are most likely weight-dependent.<sup>51</sup> However, in LORANS, blood pressure change was independent of weight, TBW, and fat mass. Similarly, Sutton et al suggested that BP reduction is not a result of weight loss in a study on intermittent fasting.<sup>70</sup>

Some authors have reported that blood pressure after Ramadan fasting returns to pre-Ramadan values.<sup>43,51,58</sup> Also, a return to baseline values was noted after intermittent fasting in an animal study.<sup>72</sup> However, 2 studies indicated larger reduction 1<sup>53</sup> and 3 months<sup>62</sup> after Ramadan fasting.

In terms of temporality, only 1 study measured SBP and DBP in 3 different time points in Ramadan to observe when BP lowering may begin.<sup>57</sup> A decline in BP was noticed after the first week of fasting. In an animal study that compared the benefits of intermittent fasting to that of caloric restriction (40% of kcals reduced), the 2 approaches were associated with reduced heart rate, SBP, and DBP during the second or third week with maximum drop in these variables by either the fourth or fifth week.<sup>72</sup>

## Heterogeneity

We observed heterogeneity ranging from low to substantial levels across subgroups and overall. This

**Fable 3.** Continued

Study	Subjects	Mean difference in SBP	MD	95%-CI	Weight
Healthy individuals Ongsara, et al. 2017 Dewanti, et al. 2006 Khan, et al. 2017 Faris, et al. 2012 Malekmaken, et al. 2017 Gupta, et al. 2013 Shehab, et al. 2013 Shehab, et al. 2012 Norouzy, et al. 2017 Sijavandi, et al. 2015 Beltaifa, et al. 2002 Martin, et al. 2004 Alsubheen, et al. 2017 Dasgupta 2017 Mohammadzad, et al. 2017 LORANS 2019 Random effects model	65 75 35 50 93 98 60 12 89 20 17 9 34 30 60		0.21 -8.99 0.48 -7.90 -2.30 -0.73 -3.54 -1.90 -0.90 0.00 -5.59 -11.00 -7.12 -3.10 -6.32	[-4.71; 5.13] [-15.35; -2.63] [-4.22; 5.18] [-11.64; -4.16] [-5.98; 1.38] [-3.43; 1.97] [-8.36; 1.28] [-8.02; 4.22] [-4.02; 2.22] [-6.20; 6.20] [-11.93; 0.75] [-21.64; -0.36] [-14.42; 0.18] [-5.68; -0.52] [-11.23; -1.41] [-4.79; -1.64]	3.5% 2.5% 3.7% 4.6% 4.6% 5.7% 3.6% 2.7% 2.6% 2.6% 2.6% 2.6% 1.1% 2.1% 5.8% 3.5% 53.8%
Heterogeneity: $l^2 = 44\%$ , $\tau^2 =$ Hypertensive individuals Norouzy, et al. 2017 Salahuddin, et al. 2014 Perk, et al. 2001 Al-Nasir & Niazi 1996 LORANS 2019 Random effects model Heterogeneity: $l^2 = 0\%$ , $\tau^2 = 0$	6 15 17 11 20		-15.50 -2.10 -6.30 -10.67	[-22.51; 13.71] [-28.93; -2.07] [-15.19; 10.99] [-31.44; 18.84] [-23.46; 2.12] [-15.16; -1.72]	0.4% 0.8% 0.8% 0.2% 0.8% 3.1%
Diabetic individuals Gholami, et al. 2019 Shao, et al. 2018 Sahin, et al. 2013 Norouzy, et al. 2012 Khan, et al. 2012 Bener & Yousafzai 2012 Yarahmadi, et al. 2003 Traore, et al. 2014 Al-Nasir & Niazi 1996 LORANS 2019 Random effects model Heterogeneity: $l^2 = 61\%$ , $\tau^2 =$	54 62 88 88 75 1301 57 25 21 12 8.5065, <i>p</i> < 0		-9.22 -0.02 -1.00 -4.39 -4.86 -4.61 13.00 -4.60 -9.83	[-10.26; 0.68] [-14.20; -4.24] [-5.60; 5.56] [-5.43; 3.43] [-9.24; 0.46] [-5.95; -3.77] [-11.64; 2.42] [ 3.52; 22.48] [-19.70; 10.50] [-19.77; 0.11] [ -6.14; -0.93]	3.1% 3.4% 3.0% 3.5% 7.4% 2.2% 1.4% 0.6% 1.3% <b>29.9%</b>
CKD patients Imtiaz, et al. 2016 Alshamsi, et al. 2016 Wan, et al. 2014 Al Wakeel 2014 Bernieh, et al. 2010 Kara, et al. 2017 Ekinici, et al. 2018 Random effects model Heterogeneity: $I^2 = 0\%$ , $\tau^2 = 0$	34 407 35 39 31 45 23 0, <i>p</i> = 0.73		1.50 1.00 0.20 -7.00 -0.70 -3.80 0.09	[-12.45; 8.25] [-1.78; 4.78] [-7.45; 9.45] [-8.66; 9.06] [-17.03; 3.03] [-12.19; 10.79] [-12.86; 5.26] [-2.42; 2.61]	1.2% 5.0% 1.7% 1.6% 1.3% 1.0% 1.5% 13.3%
<b>Random effects model</b> Heterogeneity: $I^2 = 48\%$ , $\tau^2 =$ Test for overall effect: $z = -5$ .	5.0654, p < 0 07 (p < 0.01)	01 -20 -10 0 10 20	-3.19	[ -4.43; -1.96]	100.0%

**Figure 2.** Random effects meta-analysis of Ramadan fasting on systolic blood pressure. LORANS indicates London Ramadan Study; MD, mean difference; and SBP, systolic blood pressure.

Study	Subjects	Mean difference in DBP	MD	95%-CI	Weight
Healthy individuals		: ]			
Ongsara, et al. 2017	65		-0.76	1 2 0 2 2 4 01	3.3%
	75			[-3.92; 2.40]	a sector of the
Dewanti, et al. 2006				[-12.39; -6.57]	3.5%
Khan, et al. 2017	35		1.23	• • • •	3.2%
Faris, et al. 2012	50		-4.60	[-8.32; -0.88]	2.9%
Malekmaken, et al. 2017	93		-1.40		4.7%
Gupta, et al. 2013	98		-0.28		4.3%
Shehab, et al. 2012	60		-1.03		3.1%
Norouzy, et al. 2017	12		-0.80		1.2%
Sijavandi, et al. 2015	89		-1.20		4.2%
Beltaifa, et al. 2002	20			[-9.90; -0.10]	2.1%
Martin, et al. 2004	17		-7.94	[-13.50; -2.38]	1.8%
Alsubheen, et al. 2017	9		-6.00	[-12.47; 0.47]	1.5%
Dasgupta 2017	34		-5.06	[-9.45; -0.67]	2.4%
Mohammadzad, et al. 2017	30	<u> </u>	-1.10	[-5.15; 2.95]	2.6%
LORANS 2019	60	— <b>—</b>	-3.42		3.3%
Random effects model		<b></b>	-2.82	[-4.34; -1.30]	44.2%
Heterogeneity: $I^2 = 70\%$ , $\tau^2 =$	5.4878, p < 0	0.01		h j d	
Hypertensive individuals					
Norouzy, et al. 2017	6 -		-1 10	[-14.13; 11.93]	0.5%
	15 -				2.1%
Salahuddin, et al. 2014	15 -			[-14.37; -4.23]	
Perk, et al. 2001				[-6.26; 3.26]	2.2%
Al-Nasir & Niazi 1996	11			[-13.62; 6.42]	0.7%
LORANS 2019	20			[-9.00; 0.90]	2.1%
Random effects model			-4.52	[ -7.75; -1.28]	7.6%
Heterogeneity: $I^2 = 24\%$ , $\tau^2 =$	3.2812, <i>p</i> = 0	0.26			
Diabetic individuals					
Gholami, et al. 2019	54		-0.45	[-3.92; 3.02]	3.1%
Shao, et al. 2018	62		-3.60	[-6.07; -1.13]	3.9%
Sahin, et al. 2013	88		-1.88	[-4.98; 1.22]	3.3%
Norouzy, et al. 2012	88		2.00		3.3%
Khan, et al. 2012	75		-2.88		3.5%
Bener & Yousafzai 2012	1301			[-4.55; -3.15]	5.2%
Yarahmadi, et al. 2003	57		-3.92		3.1%
Traore, et al. 2014	25		3.00		2.0%
Al-Nasir & Niazi 1996	21		-2.90	[-7.42; 1.62]	2.4%
	12				
LORANS 2019 Random effects model	12		-4.11	[-10.76; 2.53]	1.4%
Heterogeneity: $I^2 = 61\%$ , $\tau^2 =$	2 7587 p < 0	0.01	-2.13	[-3.59; -0.67]	31.2%
	,p ~ (				
CKD patients					Child Downson
Imtiaz, et al. 2016	34		-3.90		1.7%
Alshamsi, et al. 2016	407	. <b>.</b>	2.00		4.1%
Wan, et al. 2014	35		1.00	[-3.22; 5.22]	2.5%
Al Wakeel 2014	39		-0.70	[-6.98; 5.58]	1.5%
Bernieh, et al. 2010	31		-1.30	[-5.69; 3.09]	2.4%
Kara, et al. 2017	45		-0.60		1.7%
Ekinici, et al. 2018	23	<b></b>		[-4.90; 2.10]	3.0%
Random effects model				[-1.19; 1.73]	17.1%
Heterogeneity: $I^2 = 1\%$ , $\tau^2 = 0$	0.0656, p = 0.	41	w i da l	L	/u
Random effects model			-2.26	[ -3.19; -1.34]	100 0%
Heterogeneity: $I^2 = 66\%$ , $\tau^2 =$	1 1650		-2.20	[-3.18, -1.34]	100.0%
Test for overall effect: $z = -4.1$					
rest for overall effect. $z = -4$ .	r = (p < 0.01)	-10 -5 0 5 10			

**Figure 3.** Random effects meta-analysis of Ramadan fasting on diastolic blood pressure. DBP, diastolic blood pressure; LORANS, London Ramadan Study; and MD, mean difference.

heterogeneity was anticipated as the included studies were conducted in at least 18 different countries. Inevitably, this implies that the intervention (Ramadan fasting) was not the same in all studies because some crucial factors, which could influence the effect of Ramadan fasting on blood pressure, may vary from study to study. The duration of daytime (fasting hours) varies according to the latitude of the geographical location.<sup>76,77</sup> In addition, the average temperature during the day could vary depending on the geographical placement of the city or the season. Also, as the Islamic (lunar) calendar is 10 days less than the Gregorian (solar) calendar; thus, Ramadan rotates across the 4 seasons. Culture is another factor that may substantially influence individuals' lifestyle change during Ramadan, including dietary intake and physical activity. Also, some countries reduce working hours during Ramadan, which in turn reflects on the lifestyle of the whole population.<sup>78</sup> Furthermore, the difference in fasting hours is another factor that may contributed to the observed heterogeneity. A study on prediabetic individuals revealed that intermittent fasting with 18 fasting hours brings a larger reduction in SBP, DBP, and insulin levels compared with only 12 fasting hours.<sup>70</sup>

### **Clinical Implication**

Our study shows that Ramadan fasting is associated with lower blood pressure in healthy people and individuals with hypertension and diabetes regardless of their weight change during Ramadan. Treatment for these conditions needs to be kept under review during Ramadan. However, we did not find any change in blood pressure in patients with CKD, although this needs further investigation in larger sample sizes. Our results are in agreement with recommendations by Communities in Action organization (supported by the National Health Service) and the Saudi hypertension guidelines, which describe Ramadan fasting as a safe religious practice with respect to blood pressure.<sup>79,80</sup>

### **Strengths and Limitations**

This systematic review had some methodological strengths. It is the most comprehensive review on the effect of Ramadan fasting on blood pressure and incorporated quality assessment of studies in its inclusion and exclusion criteria. Although there were some previous reviews on this topic, each of them targeted studies on either healthy individuals or a specific disease group. Our meta-analysis covered studies on healthy and nonhealthy individuals and included subgroup analysis. We included our own study (LORANS) in which we recruited a multicultural community-based sample.

There are also limitations. Not all of the included studies had comprehensive data analysis. However,

conducting LORANS enabled us to demonstrate that the reductions in SBP and DBP are independent of changes in weight, TBW, fat mass, and smoking status. The dropout rate that we reported in LORANS should be acknowledged as another limitation. Nevertheless, the dropouts are not likely to have affected the overall results of LORANS because we observed no correlation between dropout rates and mean difference in SBP and DBP in the included studies as shown in Figures S11 and S12. Another limitation is that we had an indication of small-studies bias from 3 funnel plots. However, given that the magnitude and the direction of the effect were the same after using the trim and fill method to correct for the asymmetry in the 3 plots, the effect of small-studies bias is minimal. Also, participants in LORANS and the meta-analysis studies are, on average, relatively young, yet we found no association between mean age and the change in SBP and DBP as shown in Figures S9 and S10.

## CONCLUSIONS

Ramadan fasting appears to have a beneficial effect on blood pressure independent of weight, TBW, and fat mass. Our review supports the recommendations by Communities in Action organization (supported by the National Health Service) and the Saudi government, which describe Ramadan fasting as a safe religious practice with respect to blood pressure.

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#### Disclosures

None.

#### Supplementary Material

Data S1 Tables S1–S6 Figures S1–S12 References 81–84

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# SUPPLEMENTAL MATERIAL

## Selection

## 1) Representativeness of the sample: (maximum is 1 star)

a) Truly representative of the average in the target population. \* (all subjects or random sampling)

b) Somewhat representative of the average in the target population. \* (non-random sampling)

c) Selected group of users.

d) No description of the sampling strategy.

## 2) Sample size: (maximum is 1 star)

a) Satisfactory (≥100 OR ≥50 participants with power calculation). \*

b) Unsatisfactory (<100 participants without power calculation OR < 50 participants).

## 3) Non-respondents: (maximum is 1 star)

a) Comparability between respondents and non-respondents characteristics is established, and the response rate is satisfactory (response rate is  $\geq$  50%). \*

b) The response rate is unsatisfactory, or the comparability between respondents and non-respondents is unsatisfactory (response rate is < 50%).

c) No description of the response rate or the characteristics of the responders and the non-responders.

## 4) Ascertainment of the exposure (Ramadan fasting): (maximum is 2 stars)

a) Considered the number of days fasted by each participant. \*\*

b) no details of the number of days fasted.\*

## Comparability

## 1) The subjects in different outcome groups are comparable, based on the study design or analysis. Confounding factors are controlled. (maximum is 2 stars)

a) before/after design with control for main demographic factors by design. \*

b) The study controls for any additional factor (physical activity, sleep, stress or smoking). \*

## Outcome

1) Assessment of the outcome (Blood pressure): (maximum is 2 stars)

(We considered blood pressure as an universally well-measured parameter)

a) Name/model of the device used to measure the outcome reported.\*\*

b) Name/model of the device used not reported. \*

## 2) Statistical test: (maximum is 1 star)

a) The statistical test used to analyze the data is clearly described and appropriate, and the measurement of the association is presented.\*

b) The statistical test is not described or not appropriate.

We adapted this scale from the Newcastle-Ottawa Quality Assessment Scale for cohort studies <sup>24</sup> to assess the quality of selected studies in this systematic review "**The effect of religious fasting in Ramadan on blood pressure: Results from London Ramadan study (LORANS) and a meta-analysis**" as has been done in a previous study <sup>84</sup>.

Table S1: comparison between *LORANS* participants who attended the second visit and individuals who attended the first visit only.

Variable	Sub-groups	Study participants (n=85)	Individuals who didn't attend the second visit (n=61)	p-value
Age (mean ± SD)	Total	45.6 ± 15.9	39 ± 21.3 †	
	18 – 40 years (%)	31.8%	55.7%	0.002
	40 – 60 years (%)	49.4%	39.3%	
	60 – 80 years (%)	17.6%	11.5%	
	> 80 years (%)	1.2%	3.3%	
	nder le %)	52.9%	49.2 %	0.80
Ethnic background	Pakistani	16.5%	18.8%	
(%)	Indian	26.6%	35.4%	
	Bangladeshi	8.9%	6.3%	
	Somali	16.5%	22.4%	0.36
	Arab	16.5%	4.2%	
	Other	15.2%	12.5%	
	Single	22.8%	32%	
Marital status	Married/living with a partner	73.4 %	66%	0.49
(%)	Divorced/separated	3.8 %	2.1%	
With Chronic diseases	Diabetes	25.9%	13.1%	0.83
(%)	Hypertension	44.7%	13.1%	0.48
	Cardiovascular diseases	9.4%	6.6%	0.42
Education (%)	No formal qualification	12.7%	10.6%	
	Secondary school or equivalent	25.3%	19.1%	
	Higher education: College/HNC/HND	21.5%	14.9%	0.31
	Vocational qualification	1.3%	8.5%	
	Bachelor's degree	26.6%	27.7%	
	Postgraduate degree	12.7%	19.1%	
Smoking	Never	77.6%	91.5%	
(%)	Stopped	14.1%	2.1%	0.02
	Occasionally	3.5%	6.4%	0.02
	Yes, most or all days	4.7%	0%	

<sup>+</sup> median and interquartile range

# Table S2: PRISMA checklist and pages of items.

Section/topic	#	Checklist item	Reported on page #
TITLE		I	0
Title	1	Identify the report as a systematic review, meta-analysis, or both.	0
ABSTRACT	•	·	1
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	1
INTRODUCTION		·	3
Rationale	3	Describe the rationale for the review in the context of what is already known.	3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	3-4
METHODS		·	6-9
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	6
Eligibility criteria	bility criteria 6 Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.		6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	6
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	6
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	6
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	7
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	7
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	7
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	7

Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I <sup>2</sup> ) for each meta-analysis.	9
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	9
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	9
RESULTS			10-12
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	10
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	10
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	10
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	10
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	11
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	12
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	12
DISCUSSION			13,16
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	13
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	16
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	16
FUNDING	<u>.</u>		18
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	18

## Table S3: quality assessment and risk of bias in potential studies.

		Selection	ı			Outco	ome		
Studies	Representativeness	Sample size	Non-respondents	exposure	comparability	Assessment of outcome	Statistical test	Score	Quality
Ongsara, et al. 2017 <sup>31</sup>	1	1	0	1	1	2	1	7	good
Dewanti, et al. 2006 <sup>6</sup>	1	0	0	1	1	1	1	5	satisfactory
Khan, et al, 2017 <sup>30</sup>	1	0	0	2	2	1	1	7	good
Rahman, et al. 2004 56	0	0	0	1	1	1	1	4	low
Al-barha, et al. 2018 9	0	0	0	1	1	1	1	4	low
Faris, et al. 2012 32	1	0	0	2	1	2	1	7	good
Al-Nasir & Niazi, 1996 40	0	0	1	1	1	2	1	6	satisfactory
Malekmakan, et al. 2017 33	1	1	0	1	1	2	1	7	good
Khan, et al. 2012 45	1	0	0	2	1	1	1	6	satisfactory
Yarahmadi, et al. 2003 46	1	0	0	1	1	1	1	5	satisfactory
Shao, et al. 2018 42	1	1	0	1	1	1	1	6	satisfactory
Salahddin, et al. 2014 39	1	0	0	1	1	2	1	6	satisfactory
Mansi, 2007 57	1	0	0	1	1	1	0	4	low
Sahin, et al. 2013 43	1	1	0	2	1	1	1	7	good
Norouzy, et al 2012 44	1	1	0	2	1	2	1	8	good
Mansi & Amneh, 2007 55	0	0	0	1	1	1	1	4	low
Perk, et al. 2001 28	0	0	0	1	1	2	1	5	satisfactory
Shehab, et al. 2012 34	1	0	0	1	1	2	1	6	satisfactory
Alsubheen, et al. 2017 37	0	0	0	1	1	2	1	5	satisfactory
Mohammadzad, et al. 2017 38	0	0	0	2	1	2	1	6	satisfactory
Dasgupta, et al. 2017 <sup>5</sup>	1	0	0	1	1	1	1	5	satisfactory
Norouzy, et al. 2017 <sup>27</sup>	0	0	0	2	1	2	1	6	satisfactory
Wan, et al. 2014 49	1	0	0	2	1	1	1	6	satisfactory
Alshamsi, et al. 2016 48	1	1	0	1	1	1	0	5	satisfactory
Bernieh, et al. 2010 51	1	0	0	2	1	1	1	6	satisfactory
Boobes, et al. 2009 12	0	0	0	1	1	1	1	4	low
Ekinic, et al. 2018 53	1	0	0	2	1	2	1	7	good
Gholami, et al. 2018 <sup>41</sup>	0	0	0	2	1	1	1	5	satisfactory
Gupta, et al. 2013 13	0	1	0	1	1	6	1	6	satisfactory
Dwivedi, et al. 1996 59	0	0	0	1	1	1	1	4	low
Imtiaz, et al. 2016 <sup>47</sup>	1	0	0	2	1	1	1	6	satisfactory
Akturk, et al. 2013 58	0	0	0	1	1	2	0	4	low
Al-Wakeel, et al. 2014 50	1	0	0	1	1	1	1	5	satisfactory
Kara, et al. 2017 52	1	0	0	1	1	1	1	5	satisfactory
Sijavandi, et al. 2015 35	1	0	0	1	1	2	1	6	satisfactory
Traore, et al. 2014 <sup>10</sup>	1	0	0	1	1	2	1	6	satisfactory
Beltaifa, et al. 2002 <sup>29</sup>	0	0	0	2	1	1	1	5	satisfactory
Bouguera, et al. 2006 <sup>81</sup>	0	0	0	1	1	1	1	4	low
Zebidi, et al. 1990 82	0	0	0	1	1	1	1	4	low
Bouguera, et al. 2003 83	0	0	0	1	1	1	1	4	low
Martin, et al. 2004 <sup>36</sup>	0	0	0	1	1	2	1	5	satisfactory
Bener & Yousafzai, 2014 <sup>4</sup>	1	1	0	1	1	2	1	7	good
Ouziala, 1998 <sup>54</sup>	0	0	0	1	1	1	1	4	low

Table S4: estimated daytime temperature during Ramadan in 29 studies (the highest temperature during Ramadan was used as a proxy for daytime temperature).

author	Year	country	city/location	Temp. ( <sup>0</sup> C)
Ongsara, et al.	2017	Thailand	Tha Sala District	35.5
Khan, et al.	2017	Pakistan	Karachi	37
Faris, et al.	2012	Jordan	Rusaifa	34
Malekmaken, et al.	2017	Iran	Shiraz	39.5
Gupta, et al.	2013	India	Jammu city	40
Shehab, et al.	2012	UAE	Al-ain	47
Norouzy, et al. (diabetic)	2017	Iran	Mashhad	40
Norouzy, et al. (hypertensive)	2017	Iran	Mashhad	40
Sijavandi, et al.	2015	Iran	Mashhad	40
Alsubheen, et al.	2017	Canada	St. John's	27
Dasgupta	2017	India	Kolkata	40
Mohammadzad, et al.	2017	Iran	Gorgan	42
LORANS (healthy)	2019	UK	London	24
LORANS (hypertensive)	2019	UK	London	24
LORANS (diabetic)	2019	UK	London	24
Salahuddin, et al.	2014	India	Aurangabad	28
Gholami, et al.	2019	Iran	Yazd	44
Shao, et al.	2018	Singapore	Singapore.	34
Norouzy, et al.	2012	Iran	Mashhad	36
Khan, et al.	2012	Pakistan	Karachi, Pakistan	33
Bener & Yousafzai	2012	Qatar	Doha	42
Traore, et al.	2014	Mali	Bamako	34
Imtiaz, et al.	2016	Pakistan	Karachi, Pakistan	40
Alshamsi, et al.	2016	Saudi Arabia	different cities	45
Wan, et al.	2014	Malaysia	Kuala Lumpur	35
Al Wakeel	2014	Saudi Arabia	Riyadh	46
Bernieh, et al.	2010	UAE	Al-Ain	44
Kara, et al.	2017	Turkey	Rize	37.5
Ekinici, et al.	2018	Turkey	Istanbul	33.5

LORANS 2019 are presented three times as it has three subsets; Norozy et al. 2017 is presented twice as it has two subsets.

## Table S5: Further adjustments for sleep duration and energy intake.

	Before Ramadan	After Ramadan (Mean± SD)	Mean difference (95% Cl)				
	(Mean± SD)		Base Model	Second Model	Third Model	Fourth Model	
Systolic Blood Pressure	132.2± 20.1	124.9± 17.5	-7.29 (-4.74 to -9.84)* -7.30 (-4.62 to -9.95)*	-7.29 (-4.74 to -9.84)* -7.28 (-4.60 to -9.92)*	-7.22 (-4.67 to -9.85)* -7.25 (-4.57 to -9.96)*	-7.34 (-4.63 to -10.10)* -7.34 (-4.47 to -10.20)*	
			-7.63 (-4.54 to -10.72)* -7.75 (-4.48 to -10.99)*	-7.63 (-4.54 to -10.73)* -7.76 (-4.49 to -11.00)*	-7.83 (-4.69 to -10.99)* -8.02 (-4.69 to -11.33)*	-7.96 (-4.50 to -11.33)* -8.19 (-4.53 to -11.69)*	
Diastolic Blood Pressure	77.4 ± 9.7	74± 9.2	-3.42 (-1.73 to -5.09)* -3.01 (-1.33 to -4.69)* -3.76 (-1.66 to -5.86)*	-3.42 (-1.73 to -5.09)* -2.97 (-1.30 to -4.64)* -3.76 (-1.66 to - 5.86)*	-3.17 (-1.48 to -4.87) * -2.71 (-1.02 to -4.4)* -3.53 (-1.43 to -5.66)*	-3.00 (-1.19 to -4.83)* -2.56 (-0.73 to -4.4)* -3.08 (-0.78 to -5.44)*	
			-3.15 (-0.98 to -5.31)*	-3.16 (-1.00 to -5.31)*	-2.88 (-0.71 to -5.05)*	-2.47 (-0.07 to - 4.86)*	

Base Model adjusts for age, gender, site & 2nd measurement day Second model adjusts for Base model variables & smoking status Third model adjusts for Second model variables & weight Fourth model adjusts for Second model variables, total body water & fat-mass \* p-value <0.001 Beta and Cl in red= adjusting further for sleep duration (n=80)

Beta and CI in blue= adjusting further for energy intake (n=55)

Beta and CI in green = adjusting further for sleep duration and energy intake

Table S6: risk of bias tests

Subgroup		Egger test p-value	p-value using Trim & fill	MD using trim & fill	Original p-value	Original MD
Healthy	SBP	0.14	NA	NA	NA	NA
	DBP	0.15	NA	NA	NA	NA
Diabetic	SBP	0.40	NA	NA	NA	NA
	DBP	0.05	<0.001	- 3.67	<0.01	- 2.13
Hypertensive	SBP	0.70	NA	NA	NA	NA
	DBP	0.77	NA	NA	NA	NA
СКД	SBP	0.07	0.26	1.30	0.73	0.09
	DBP	0.05	0.10	1.45	0.41	0.27
All studies	SBP	0.63	NA	NA	NA	NA
combined	DBP	0.33	NA	NA	NA	NA

NA: not applicable.

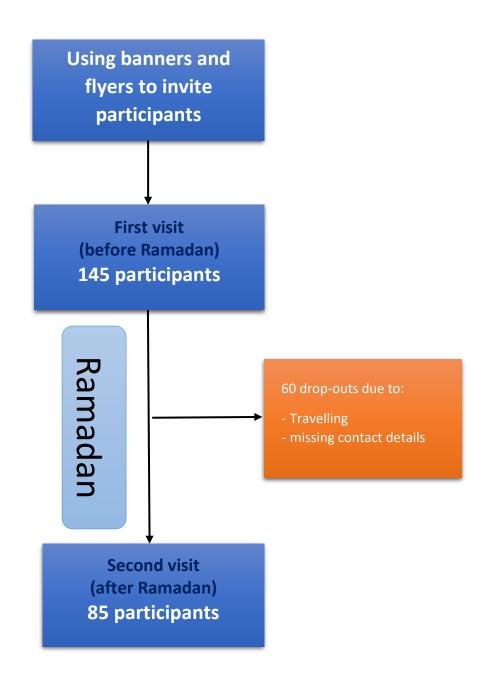


Figure S1: flowchart of participants attendance to the first and the second visit in LORANS.

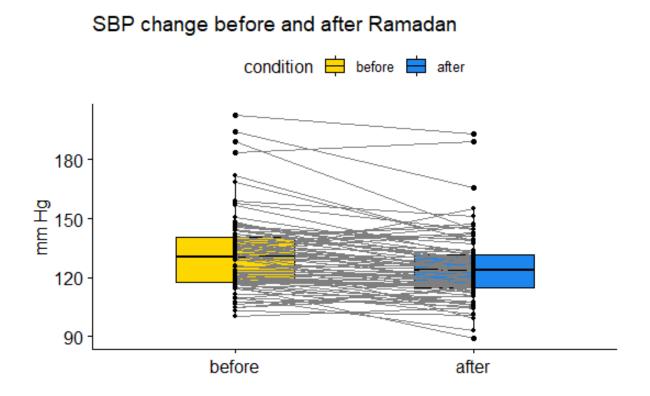


Figure S2: SBP before and after Ramadan fasting in LORANS, 2019.

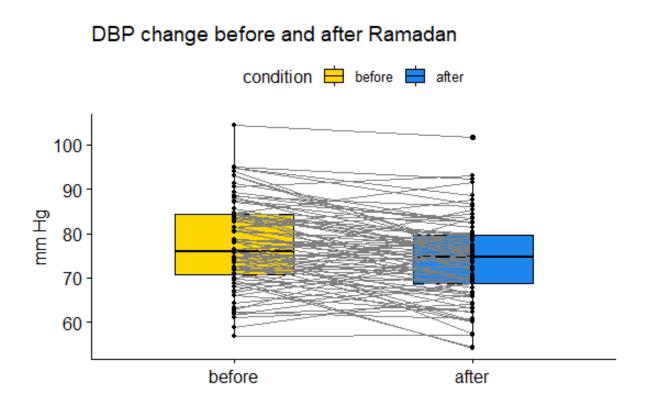


Figure S3: DBP before and after Ramadan fasting in LORANS, 2019.

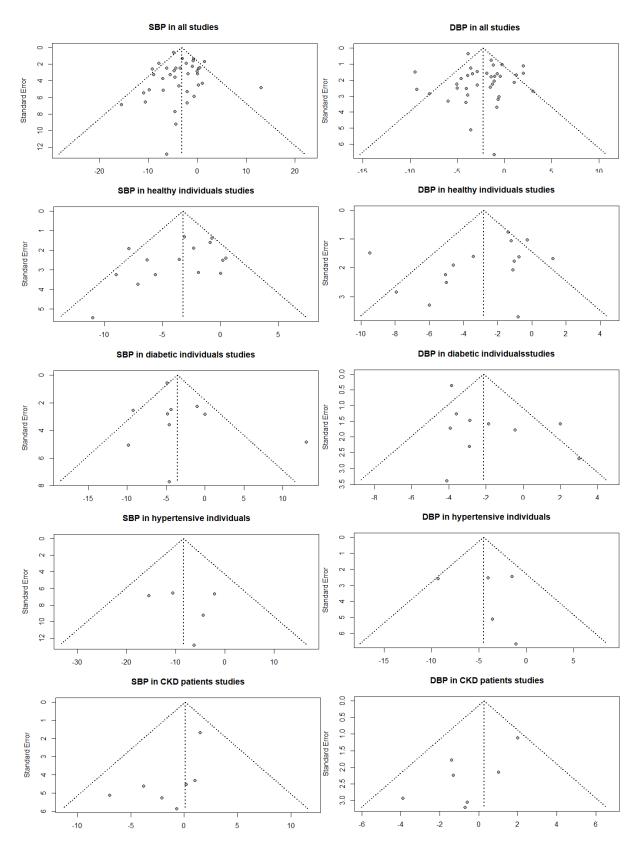


Figure S4: funnel plots of SBP and DBP in all studies and subgroups.

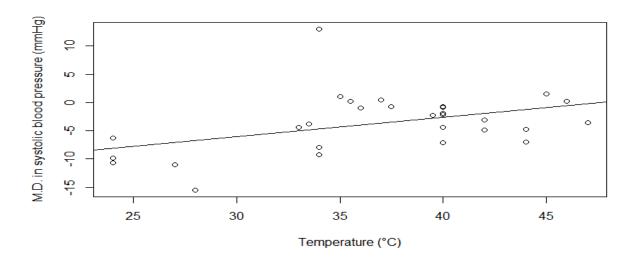


Figure S5: regression analysis of SBP changes according to temperature during Ramadan and mean difference values in 29 studies.

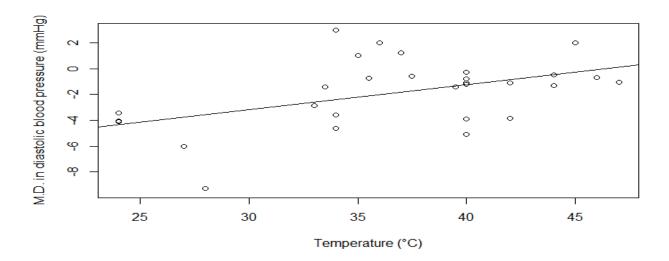


Figure S6: regression analysis of DBP changes according to temperature during Ramadan and mean difference values in 29 studies.

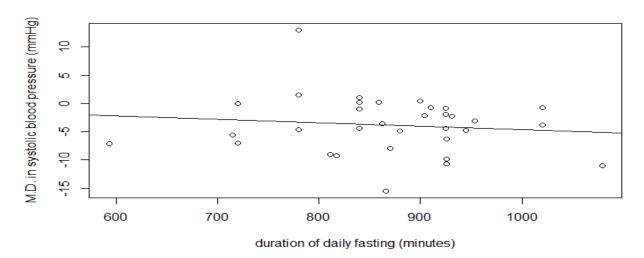


Figure S7: regression analysis of SBP changes according to the duration of fasting per day (minutes) during Ramadan and mean difference values in 33 studies.

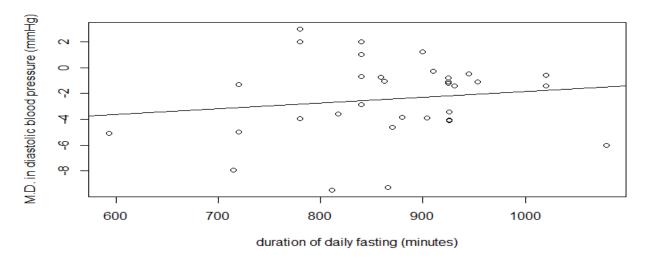


Figure S8: regression analysis of DBP changes according to the duration of fasting per day (minutes) during Ramadan and mean difference values in 33 studies.

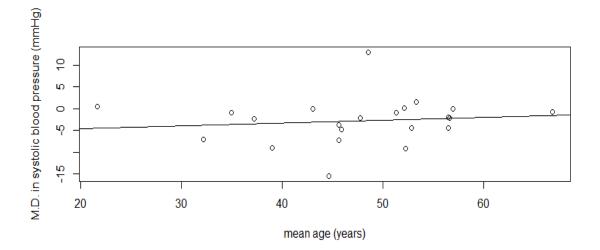


Figure S9: regression analysis of SBP changes according to the mean age of participants (years) and mean difference values in 22 studies.

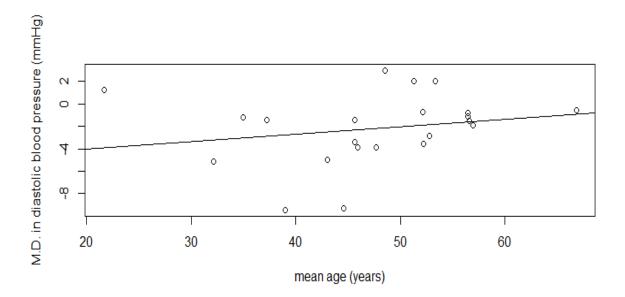
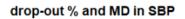


Figure S10: regression analysis of DBP changes according to the mean age of participants (years) and mean difference values in 22 studies.



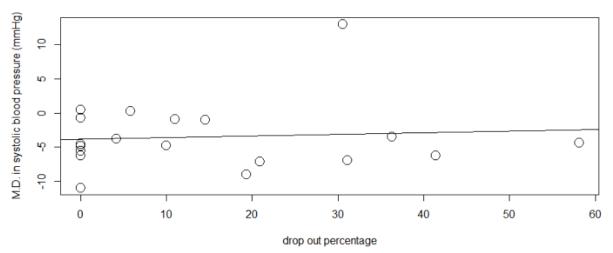


Figure S11: regression analysis of mean difference in SBP changes according to the drop-out percentages in 19 studies.

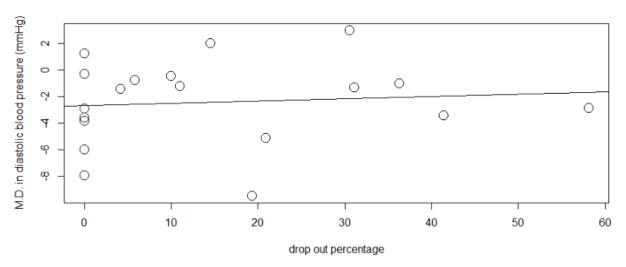


Figure S12: regression analysis of mean difference in DBP changes according to the drop-out percentages in 19 studies.