

# Assessing the Renal Safety and Functional Outcomes of Creatine Supplementation

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## Abstract

Creatine monohydrates are among the most extensively investigated nutritional supplements and is frequently used to enhance exercise capacity, support muscle performance, and aid rehabilitation in various clinical settings. Despite its well-established efficacy, questions remain regarding its renal safety because creatine supplementation may increase serum creatinine concentrations, potentially leading to misinterpretation of kidney function. This systematic review and meta-analysis was undertaken to critically evaluate the available evidence on the effects of creatine supplementation on key indicators of renal function.

**Keywords:** Creatine monohydrate; creatine supplementation; renal function; kidney safety; serum creatinine; glomerular filtration rate; estimated GFR; systematic review; meta-analysis; nutritional supplements.

## Introduction

Creatine monohydrate is one of the most widely studied and utilized nutritional supplements, valued for its well-documented ability to enhance exercise performance, support muscle strength, and aid recovery across both athletic and clinical populations (1). Despite decades of research affirming its efficacy, concerns about its renal safety have persisted, largely because creatine supplementation can raise serum creatinine levels, a biomarker conventionally used to assess kidney function, raising the possibility of misdiagnosed renal impairment in otherwise healthy individuals. Isolated case reports of interstitial nephritis and renal dysfunction associated with creatine use have further fueled this apprehension, even as

larger controlled trials have generally reported no adverse effects on measures like glomerular filtration rate. Given this persistent tension between anecdotal safety signals and the broader body of clinical evidence, a systematic and quantitative synthesis of the available literature is warranted to clarify whether creatine supplementation genuinely compromises renal function or whether observed changes in serum creatinine simply reflect its role in creatine metabolism. This systematic review and meta-analysis therefore aim to critically evaluate the effects of creatine supplementation on key renal outcomes, namely serum creatinine and glomerular filtration rate, across studies published between January 2000 and March 2024.

## Review

A systematic search of PubMed, Scopus, Web of Science, and Google Scholar was performed to identify eligible studies published between January 2000 and March 2024 (2). Randomized controlled trials and prospective clinical studies evaluating the effects of creatine supplementation on renal function in healthy individuals or clinical populations were considered. The primary outcomes included serum creatinine concentration and estimated or measured glomerular filtration rate (GFR). Data were synthesized using random-effects meta-analysis, and subgroup analyses were conducted according to the duration of supplementation to explore temporal differences in treatment effects (3) (Table 1).

Twenty-one studies fulfilled the eligibility criteria for systematic review, while 12 studies comprising 440 participants (177 receiving creatine supplementation and 263 controls) contributed to the quantitative synthesis of serum creatinine. Pooled analysis demonstrated a modest but statistically significant increase in serum creatinine among participants receiving creatine compared with controls (mean difference: 0.07; 95% confidence interval: 0.01–0.12;  $p = 0.03$ ) (4). The increase was most evident during the initial week of supplementation and reappeared in studies with prolonged supplementation beyond 12 weeks, whereas no significant differences were observed during intermediate treatment periods. In contrast, pooled estimates showed no

| Study Characteristic                  | Description                                                |
|---------------------------------------|------------------------------------------------------------|
| Total studies screened                | 1,124                                                      |
| Full-text articles assessed           | 54                                                         |
| Studies included in systematic review | 21                                                         |
| Studies included in meta-analysis     | 12                                                         |
| Total participants (meta-analysis)    | 440                                                        |
| Creatine supplementation group        | 177                                                        |
| Control group                         | 263                                                        |
| Study design                          | Randomized controlled trials, prospective clinical studies |
| Publication period                    | January 2000 – March 2024                                  |
| Databases searched                    | PubMed, Scopus, Web of Science, Google Scholar             |
| Primary renal outcomes                | Serum creatinine, estimated/measured GFR                   |
| Supplementation duration              | ≤1 week to >12 weeks                                       |
| Statistical model                     | Random-effects meta-analysis                               |
| Subgroup analysis                     | Based on duration of supplementation                       |

**Table 1:** Summary of Studies Included in the Systematic Review.

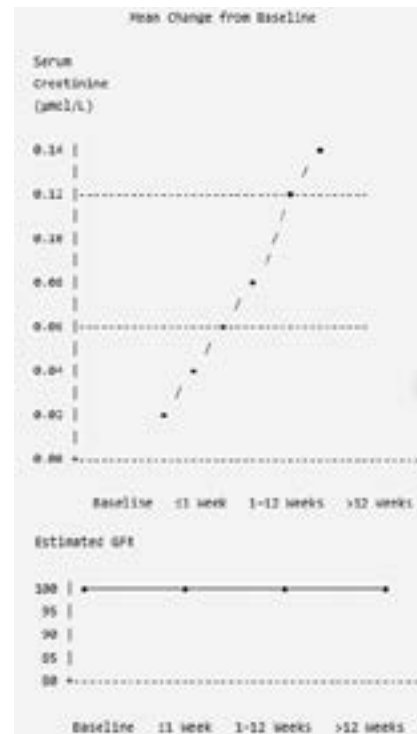


**Figure 1:** Overall Effect of Creatine Supplementation on Renal Function (Black-and-White Graph).

statistically significant effect of creatine supplementation on GFR, indicating that filtration capacity remained stable throughout the intervention periods (5,6) (Figure 1).

Black-and-white line graph illustrating the temporal changes in serum creatinine and estimated glomerular filtration rate (GFR) following creatine supplementation. Serum creatinine shows a modest increase during the early phase of supplementation and after prolonged use, whereas estimated GFR remains relatively stable across all follow-up periods, indicating preserved renal function.

## Conclusion

Current evidence suggests that creatine supplementation does not adversely affect renal function in healthy individuals or the populations examined. Although supplementation may produce a slight elevation in serum creatinine, this finding most likely reflects increased creatine metabolism rather than a decline in kidney function. The absence of significant changes in GFR supports the renal safety of creatine supplementation when consumed within recommended dosages. Nevertheless, additional large-scale, long-term randomized clinical trials involving individuals with pre-existing kidney disease are warranted to further establish its safety profile.

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