# INPLASY PROTOCOL

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**Conflicts of interest:**
**None declared.**

# The effectiveness of high-dose intravenous vitamin C for patients with coronavirus disease 2019: A systematic review

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**Review question / Objective:** **Vitamin C has anti-inflammatory effects. This review aimed to investigate the therapeutic effect of high-dose intravenous vitamin C (HDIVC) in patients with coronavirus disease 2019 (COVID-19).**
**Condition being studied:** **Since the first confirmed case of the COVID-19 in late 2019, COVID-19 has rapidly spread worldwide in just 2-3 months and eventually became a global health issue. We present the effectiveness of vitamin C in the treatment of COVID-19 with this review. Vitamin C has antioxidant properties that increases in patients with infection, which frequently reduces vitamin C levels, and in patients with pneumonia or critical illness, it suppresses inflammation and improves immunoregulatory function. HDIVC has also been administered in patients with COVID-19 in many previous studies that evaluated the effectiveness of HDIVC in patients with COVID-19 in different settings with various clinical findings and results. Previous studies have yielded not only similar findings but also contradictory findings, and thus the therapeutic effects of HDIVC in COVID-19 patients remain unclear.**

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 17 September 2021 and was last updated on 17 September 2021 (registration number INPLASY202190051).

## INTRODUCTION

**Review question / Objective:** **Vitamin C has anti-inflammatory effects. This review aimed to investigate the therapeutic effect of high-dose intravenous vitamin C (HDIVC) in patients with coronavirus disease 2019 (COVID-19).**

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## METHODS

**Search strategy:** Articles published between January 1, 2019, and July 29, 2021, were searched in the PubMed, Cochrane, Embase, and Web of Science databases using the following key phrases: "Vitamin C OR ascorbic acid" AND "COVID-19 OR coronavirus disease 2019 OR severe acute respiratory syndrome coronavirus 2 OR SARS-CoV-2.".

**Participant or population:** Patients with COVID-19.

**Intervention:** Treatment using HDIVC.

**Comparator:** Standard care only without HDIVC.

**Study designs to be included:** We included the randomized controlled trials, retrospective studies.

**Eligibility criteria:** Studies that used HDIVC for the management of patients with COVID-19.

**Information sources:** The studies were searched in the PubMed, Cochrane, Embase, and Web of Science databases.

**Main outcome(s):** All available outcomes mentioned in the included studies, they were mortality rate, length of hospital stay.

**Quality assessment / Risk of bias analysis:** Quality assessment for randomized trials was conducted using the Cochrane Collaboration tool and for retrospective studies, using the Newcastle-Ottawa quality assessment scale.

**Strategy of data synthesis:** Data for meta-analysis were independently investigated by two researchers (M.C.C and Y.H.C). Discrepancies were resolved through discussion. The extracted data were analyzed using Comprehensive Meta-Analysis version 2 (Biostat Inc., Englewood, NJ, USA).

**Subgroup analysis:** Not applicable.

**Sensitivity analysis:** Not applicable.

**Language:** English.

**Country(ies) involved:** Republic of Korea.

**Keywords:** Vitamin C; Ascorbic acid; SARS-CoV-2; COVID-19; Inflammation.

**Contributions of each author:**
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