Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Original article

Investigating of the role of CT scan for cancer patients during the first wave of COVID-19 pandemic

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1. Introduction

The COVID-19 pandemic has dramatically changed medical, economic, and social practices worldwide. In early 2020, the virus spread quickly around the globe, rapidly contributing to the largest pandemic outbreak since the great influenza crises of 1918 and 2009 [1]. This pandemic has had a disproportionate impact on healthcare systems, both directly by overloading hospitals with COVID patients and indirectly by modifying how unaffected patients—those without an active COVID infection—are managed. While these consequences have been sparsely investigated in pediatric [2] and pregnant [3] populations, there is an overall paucity of research in this area and many studies are burdened by limitations such as the use of purely retrospective patient cohorts. Moreover, there are even fewer studies evaluating the lasting effects of the pandemic on cancer patients specifically [4], despite the fact that cancer remains a leading cause of death worldwide. As cancer treatments continue to improve, and the population of "chronic" oncologic patients grows, it will be of utmost importance to improve detection of emergent diseases in the setting of pre-existing cancer.

With COVID-19, as with many diseases of the 21st century, there exists a central role for imaging in diagnosis, management, and prognostication. Chest Computed Tomography (CT), in particular, has demonstrated potential clinical utility due to its accessibility, speed, and relatively high diagnostic sensitivity for COVID-19 detection, ranging from 61% [5] to 99% [6]. Specificity is also promising, though a bit more controversial, with recent studies indicating performances up to 91% [7], dramatically improved from older publications hovering around 25% [8]. It is important to note that these metrics are achieved in the absence of underlying disease, in patients with a presumed "normal" pre-infection CT appearance of pulmonary parenchyma. In theory, pre-existing parenchymal abnormalities, like those widely observed in cancer patients, or related drug-induced pulmonary changes, may compromise the performance of chest CT in diagnosing active COVID-19 infection. However, how exactly this underlying disease impacts imaging performance is yet to be fully explored, and thus the applicability of diagnostic chest CT remains disputed [9, 10] and seen less favorably than the gold standard of RT-PCR. The main objective of the present study, conducted during the first wave of the COVID-19 pandemic, is to perform a systematic review and meta-analysis comparing the performance of chest CT for the diagnosis of COVID-19 in patient populations with and without cancer.

2. Materials and methods

2.1. Study selection and literature search strategy

The study protocol was developed and previously registered in PROSPERO with the following registration number CRD42020184819.

For our purposes, a systematic search of the major reference database MEDLINE (PubMed), was undertaken in April 2020. Two major imaging databases built for the COVID-19 pandemic, Radiology [11] and European Radiology [12], were also included in the search. The study was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Key search terms included "CT" AND "COVID-19". Details of search terms used for each database are reported in Table 1. All articles from 01/

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Table 1
Search Strategy for MEDLINE (Pubmed).

Keywords	("CT findings" OR "CT scan" OR "CT-scan") AND ("COVID-19"OR "COVID19″ OR "COVID 19")
Publication period	01/02/20 – 04/23/20

02/2020 to 04/23/2020 were screened. After removal of duplicate articles and publications including only an abstract, we automatically excluded reports that were not in English or that were non-human studies, case reports with less than 5 patients, systematic or non-systematic reviews, comments, correspondences, editorials, guidelines, and meta-analyses. The commercial bibliographic management software used was EndNote X9.3.1.

2.2. Inclusion and exclusion criteria

Titles and abstracts of articles were initially screened to select eligible publications, and we removed those with the following characteristics: (1) Publications with data other than imaging; (2) Abstracts

Table 2
Extracted relevant data.

General publication data	Title
	Authors
	Journal
	Date of publication
	Country
Study design and characteristics	Retrospective study
	Prospective study
	Case report / ncase series
	Editorial
	Consensus conference
	Correspondence / comment
	Review / Meta-analysis
	Monocentric
	National multicentric
	International multicentric
Population	Percentage of oncologic patients
	Specific population (pediatric – pregnant)
Diagnostic performance	Sensitivity
	Specificity
	TP/FP/FN/TN

Abbreviations: CT:computed tomography, TP: true positives, FP: false positives, FN: false negatives, TN: true negatives.

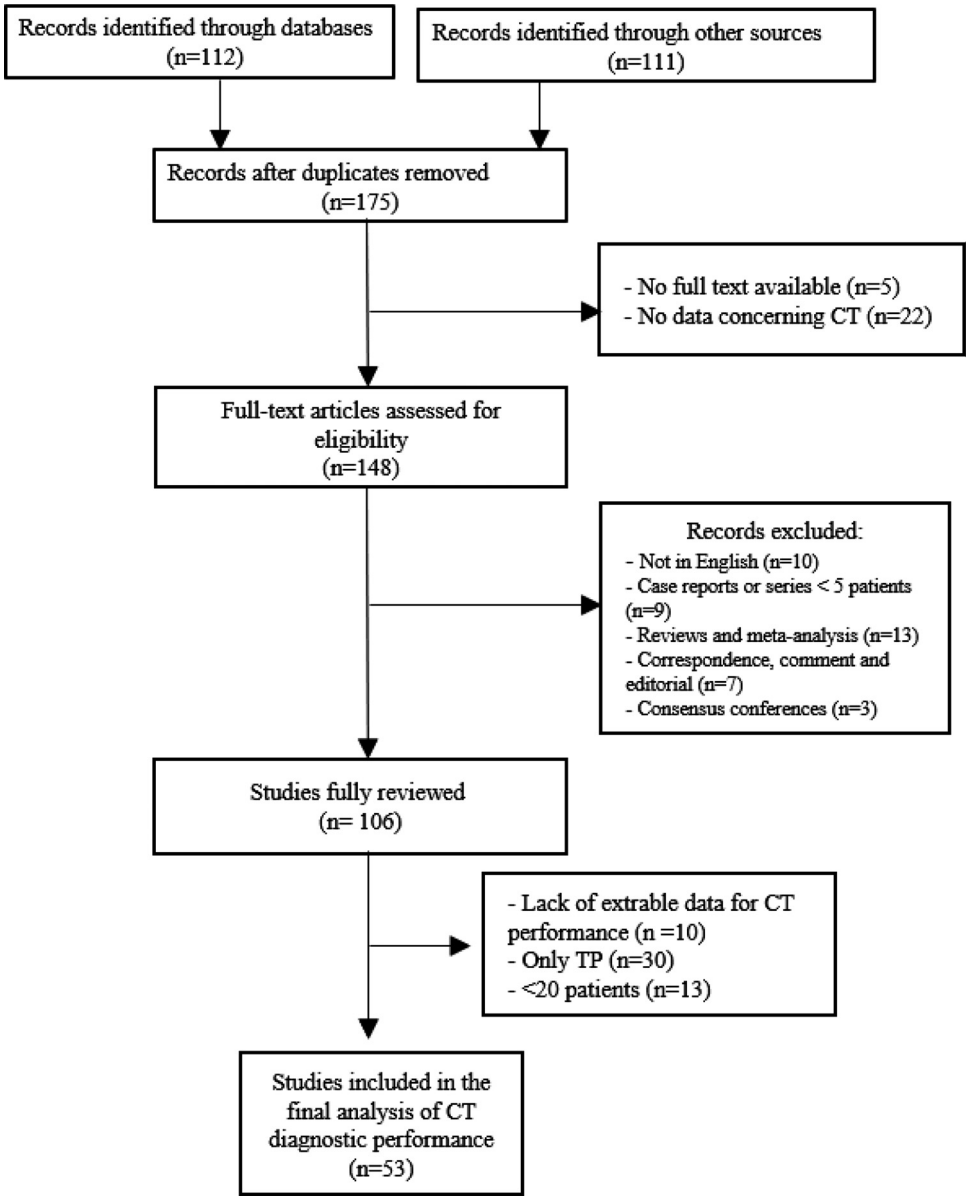

Fig. 1. PRISMA flowchart.

with unavailable full-text versions; (3) Studies investigating the diagnostic value of ultrasound (US), chest X-ray or other imaging modalities; (4) Studies focused on pregnant women or newborns.

All studies identified by the search were screened for eligibility by two independent authors (S.B and F.Z.M) blinded to each other's decisions. In case of disagreement, a consensus was reached by a third reviewer (E.P)

2.3. Data extraction

Two reviewers (S.B and F.Z.M) extracted the following data from each selected imaging-based article: (1) Authors, journal and year of publication, country of origin; (2) Study design characteristics; (3) Demographics as well as clinical and pathological variables with percentage of cancer patients if available; (4) Imaging performance metrics such as sensitivity, specificity, and contingency tables. Table 2 summarizes all extracted data. The two investigators (S.B, F.Z.M) assessed all studies independently. Disputes were discussed with a third reviewer (L.D) and resolved by consensus.

2.4. Data analysis

The sensitivity and specificity of chest CT were pooled separately using a random-effects model. The positive predictive value (PPV) and negative predictive value (NPV) of CT as a diagnostic test was estimated for a wide range of disease prevalence rates. Studies without extractable data were excluded from the meta-regression analysis. Sensitivity analysis was conducted for chest CT. Additionally, all duplicate studies were removed.

2.5. Statistical analysis

Analyses were conducted using Microsoft Excel (v2019, Microsoft, USA, 2019) and open-source R software (version 3.6.2; R Foundation for Statistical Computing, Vienna, Austria). A p-value less than 0.05 was considered indicative of statistical significance ($\alpha = 0.05$).

3. Results

3.1. Identification and selection of studies

Our literature search resulted in 175 unique studies after removal of duplicates. Records that included only an abstract ($n = 5$), were non-English and did not have extractable imaging data ($n = 10$), and those that had no imaging data at all ($n = 22$) were automatically excluded. We screened the remaining studies and removed case reports or series of less than 5 patients ($n = 9$), correspondences, comments, and editorials ($n = 7$), consensus conferences ($n = 3$), and reviews/meta-analyses ($n = 13$). In total, 106 publications fulfilled our search criteria and were fully reviewed. For our analysis of diagnostic accuracy, we further curated the studies under consideration. Of the 106 surveyed, 96 had extractable data for a two-by-two contingency table of diagnostic performance, but 30 of these were removed as they only reported the true-positive number of patients. Additionally, 13 studies that included fewer than 20 patients were removed to improve statistical significance, leaving 53 reports for our final analysis [3,5,6,8,13–61], (Supplementary table A). The PRISMA flowchart of literature search and study selection process is shown in Fig 1.

Among the publications identified for diagnostic accuracy evaluation, 92% (49/53) were retrospective studies, 4% (2/53) were case reports/case series with more than 5 patients, and only 4% (2/53) were prospective studies. Most of the reviewed works ($n = 41/53$, 77%) were monocentric and locally based. Moreover, only 23% ($n = 12$) were national multicenter studies and only one was multinational.

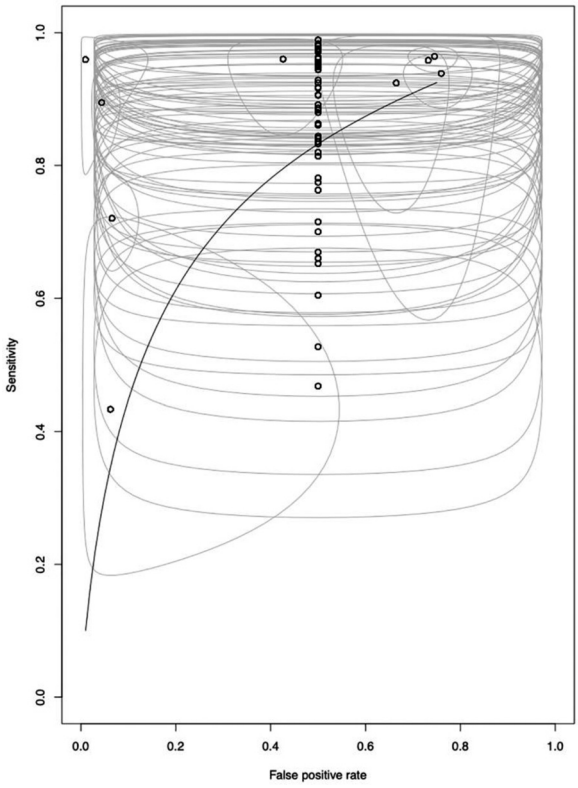

Fig. 2. ROC curve of chest CT for diagnosis of COVID-19., The pooled performance was estimated (black line). The pooled false positive rate is displayed as a function of pooled sensitivity (black line). The FPR and Se for each study are displayed (dots) as well as their estimated 95 confidence intervals (gray line).

3.2. CT diagnostic performances

Of the 53 studies reviewed for diagnostic accuracy, 6 presented data on two different populations, allowing performance calculations to be carried out for each cohort individually. Overall, our analysis of chest CT sensitivity for the detection of COVID-19 pneumonia showed promising results: In 51% of cases (30/59), the sensitivity was found to be above 0.9, with varying confidence intervals (Fig 2). However, chest CT specificity remained low at just 0.565 (IC95 [0.539; 0.591]). In 93% of cases (55/59), a specificity lower than or equal to 0.5 was reported (Fig 3).

3.3. Oncologic population

Only 15 of the original 106 reports (14.2%) identified in our search discretely included cancer patients; 92 (86.8%) made no mention of cancer rates in their study populations and subsequently failed to demarcate these patients within the data, 1 study (0.9%) identified and excluded cancer patients while 13 (12.2%) indicated the presence of cancer in their cohorts but without further details. Finally, 3 studies (2.8%) pertained specifically to oncologic populations, but none were included in the final analysis due to only reporting true positives ($n = 2$) or outright lack of performance data ($n = 1$). Overall, only 7 studies that included and described cancer patients were included in the final analysis for chest CT performance. The aggregate prevalence of cancer across all studies surveyed was 0.3% (34/11,352 patients), with absolute numbers in individual reports ranging from 1 to 17 patients. Therefore, a specific analysis of chest CT performance in the oncologic population could not be done.

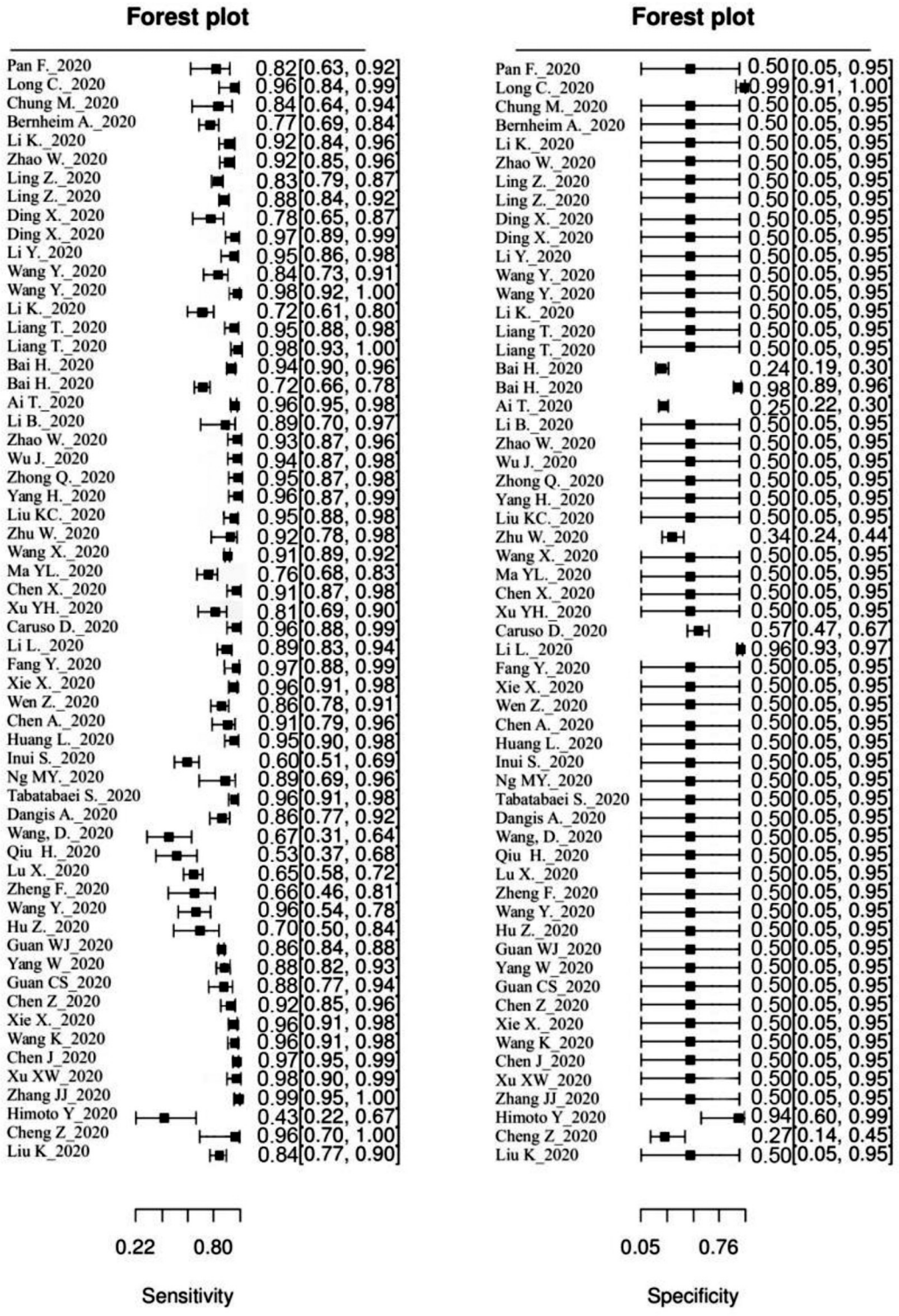

Fig. 3. Forest plots of sensitivity and specificity of chest CT for the diagnosis of COVID-19., The Sensitivity and Specificity for each study is displayed as well as their estimated 95 confidence interval.

4. Discussion

In this systematic review and meta-analysis on chest CT imaging for the diagnosis of COVID-19 pneumonia, performed from 01/02/2020 to 04/23/2020 with a special focus on oncologic populations, our main finding was that there exists a dearth of research specifically addressing cancer patients. Among the 53 articles included in our performance analysis, sensitivity of chest CT was 0.889, with a low specificity of 0.565 (IC95 [0.539; 0.591]), falling below 0.5 in 90% of studies. Moreover, only 7 articles (7/53, 13%) specifically mentioned oncology patients in their results, rendering an evaluation of chest CT performance in this population impossible to conduct. The number of cancer patients in the individual studies included in our meta-analysis varied between 1 and 17 patients, for an aggregate total of 34 patients (0.3% of 11,352 patients included). Cancer prevalence in these cohorts was therefore much lower than the global

figure of 5.8% reported in WHO statistics [62]. Among all reviewed studies, only one (1/106, 1%) specifically reported performance in the cancer patient group, but unfortunately only reported true positive patients, precluding further analysis. Our results are consistent with existing literature which has confirmed the high sensitivity of CT for the diagnosis of COVID-19, ranging from 89.76% (CI95 [84.42%; 93.84%]) to 94.6% (CI95 [91.9%; 96.45%]) [63,64]. More recent literature, published after completion of our study, shows improved values for specificity ranging from 87.2% (CI95 [83.9%; 89.9%]) to 91% (CI95 [91%; 92%]) [7,65]. Of note, these studies do not detail the prevalence of cancer in their study populations.

Several challenges regarding cancer management have arisen in the era of COVID-19. Primarily, although still poorly defined, the incidence of COVID-19 appears to be almost doubled in oncology populations when compared to the general population [66,67], with cancer patients facing a higher risk of severe disease manifestation requiring invasive airway management. This problem is compounded by the relatively older age of cancer patients, as age correlates with a higher frequency of hospitalization and severe disease [66,67], and the increased likelihood of COVID-19 exposure associated with frequent hospital visits for disease monitoring and treatment [68]. Moreover, the immunocompromising nature of both cancer and the associated treatment may make patients more susceptible to infections, though this point remains controversial as the estimated probability of death in infected patients with cancer ranges broadly from 13% to 33.1% [69,70]. Some studies have even reported similar death rates between cancer and non-cancer groups [71]. Finally, as a result of the pandemic, the quality of oncological care may suffer due to cancelation or postponement of non-urgent procedures and examinations, with possible consequences for patients who are lost to follow-up. According to a survey by the American Cancer Society Cancer Action Network (ACSCAN) during the first wave of COVID-19, 27% of patients undergoing active cancer treatment reported an interruption of a care, of which one out of five was related to a follow-up imaging exam [72]. In light of these findings, it is clear that the principle dilemma for oncologists has been the prioritization of tests and follow-up, balancing risk and benefit in the context of the ongoing pandemic [73]. Recommendations by national and international societies can shed light on some of these difficult situations [74–76], and radiologists in particular may emerge as leading figures in pandemic management for oncology patients. The latter must learn to expertly recognize COVID-19 pneumonia, meet the expectations of each clinical contact, particularly in the context of oncology, and prioritize examinations according to individual cases. They must also be familiar with all possible differential diagnoses relating to a clinical situation and must be cognizant of the possibility for incidentalomas [77]. Above all, they must reorganize and adapt to the new proposed care pathway and create reports within the current medical landscape defined by COVID-19. This last piece may prove to be the most challenging, considering the torrent of often contradictory recommendations being published at an ever-increasing pace by national and international bodies.

The role of chest CT for the initial management of COVID-19 patients without underlying cancer is currently well established, guided by relatively homogenous international recommendations [78]. Although most patients now arrive at the emergency room with a positive PCR, the usefulness of CT remains steadfast, allowing for correction of possible false negatives, assistance in the construction of differential diagnoses, and orientation of patients with prognostic information [79]. The current study suffers from a few limitations. First, the date range of our survey only covers the first wave of pandemic. Since this time, and as described above, the role of CT has slowly evolved due to the improved availability of antigenic and PCR testing. In addition, it would be useful to have more information available about the specific cancer cases described in the literature, including the date of diagnosis, whether or not it was active disease, and the treatment in progress. These additional pieces of data could be correlated with CT diagnostic performance. In conclusion, this meta-analysis highlights the lack of data concerning radiologic evaluation of COVID-19 cases in patients with underlying cancer. Further studies are required for this nuanced and highly sensitive population in order to better understand the specific performances of imaging techniques, and thereby lead to the improvement of disease management.

Declaration of Competing Interest

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

CRediT authorship contribution statement

Sylvain Bourdoncle: Investigation, Writing – original draft, Resources. **Thomas Eche:** Writing – review & editing, Resources. **Jeremy McGale:** Writing – review & editing. **Kevin Yiu:** Writing – review & editing. **Ephraïm Partouche:** Methodology, Writing – review & editing. **Randy Yeh:** Writing – review & editing, Resources. **Samy Ammari:** Writing – review & editing, Resources. **Hervé Rousseau:** Validation. **Laurent Dercle:** Conceptualization, Methodology, Data curation, Software, Formal analysis, Writing – review & editing. **Fatima-Zohra Mokrane:** Conceptualization, Methodology, Supervision, Writing – review & editing.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.redii.2022.100004.

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