



# Systematic Review The Association of Health Literacy with Intention to Vaccinate and Vaccination Status: A Systematic Review

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Abstract: Despite health literacy (HL) being recognized as a driver of health-promoting behavior, its influence on the vaccination decision-making process remains unclear. This study summarized current evidence on the association between HL and both intention to vaccinate and vaccination status. We searched PubMed, Scopus, and Web of Science, retrieving observational studies published until January 2022 that used HL-validated tools to investigate the above associations for any vaccine. Quality was assessed using the Newcastle–Ottawa scale. Twenty-one articles were included; of these, six investigated the intention to vaccinate and the remainder vaccination status. Articles on intention looked at SARS-CoV-2 vaccination using heterogeneous HL tools and were of high/fair quality. Vaccination status, mainly for influenza or pneumococcal vaccines, was explored using various HL tools; the quality was generally high. We found inconsistent results across and within vaccine types, with no clear conclusion for either vaccination intention or status. A weak but positive association was reported between a high HL level and influenza vaccination uptake for individuals aged more than 65 years. HL did not seem to significantly influence behavior towards vaccination. Differences in the methods used might explain these results. Further research is needed to investigate the role of HL in the vaccination decision-making process.

Keywords: health literacy; vaccination; systematic review; vaccine

# 1. Introduction

Vaccines are one of the most effective and cost-effective tools for the primary prevention of infectious diseases [1]. They provide immunity against various illnesses, preventing death and disability in vaccinated individuals, but also protecting those who cannot be immunized by the attainment of herd immunity [2]. Despite their unquestionable success [3], immunization coverage for several diseases has plateaued or even dropped over the last decade [4]. In Europe, for example, only a few countries have reached the immunization coverage target of 95% against measles [5], and none has achieved an uptake of 90% for the final dose of the human papillomavirus (HPV) vaccine [6]. Key challenges to the attainment of such immunization goals have been unequal access to vaccine services, which particularly affects vulnerable populations, and vaccine hesitancy, a phenomenon that has attracted worldwide interest [7–9]. In addition, the COVID-19 pandemic has negatively impacted routine immunization services in most countries, interrupting vaccination demand and supply [10], with consequences yet to be fully quantified [11].

In this context, identifying the factors that might influence vaccination uptake has been the subject of intense research [9,12–15]. One possible factor is health literacy (HL), which is a driver of population empowerment that may contribute to a reduction in health inequality [16–18]. Health literacy is also inextricably linked to the social and cultural context, which includes education, and it depends on the healthcare system organization, with all these aspects varying across countries [17]. A recent update to the definition of HL has emphasized its role in improving the health and well-being of people, underlining



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**Copyright:** © 2022 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (https:// creativecommons.org/licenses/by/ 4.0/). the importance of individual engagement in reaching this goal and acknowledging the fact that organizations need to address it equitably [19,20]. Besides being considered an independent determinant of an individual's health, HL also has a role in mediating the association between socioeconomic status and specific health outcomes, health-related behavior, and access to and use of health services [19,21]. Indeed, it has been demonstrated that people with low HL levels more frequently have poor health outcomes, such as increased hospitalization, higher rates of medication nonadherence, and a lower uptake of preventive interventions [21].

Nevertheless, while HL is a predictor of participation in cancer screening programs [22], a clear relationship between HL and vaccination behavior has not yet emerged [23]. In fact, despite the growing number of studies that have investigated the influence of HL on an individual's behavior towards vaccination [23,24], there are few reports of HL being a determinant [23]. In addition, factors including heterogeneity in the outcomes investigated and the instruments used for assessment, as well as differences in the vaccine type and the target populations, have made it difficult to generalize the results [23,25,26]. Therefore, the aim of this systematic review was to update and summarize findings on the association between HL and vaccination behavior. We considered both intention to vaccinate and vaccination status, aiming to provide a comprehensive picture of the vaccination decision-making process and to support the implementation of public health strategies that promote vaccination uptake.

#### 2. Materials and Methods

This study was performed according to the Cochrane Handbook for Systematic Reviews and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [27,28]. The review protocol was registered at PROSPERO (identifier CRD42022302724). Because this study did not involve primary data collection, the protocol was not submitted for institutional review board approval and did not require informed consent.

#### 2.1. Search Strategy and Study Selection

Three reviewers searched the bibliographic databases PubMed, Web of Science and Scopus using the following search string: ("health" AND "literacy") OR ("health literacy" OR "health literacy [MeSH Terms]") AND ("vaccin\*" OR "immuniz\*" OR "immunis\*" OR "vaccination [MeSH Terms]" OR "vaccines [MeSH Terms]"). The string was adapted to fit the search criteria of each database (Supplementary Table S1). The search was conducted among reports published from database inception to 11 January 2022. No language or date restriction was applied. Duplicate articles were removed, and the title and abstract of all retrieved records were screened. Studies that did not meet the inclusion criteria were excluded. Full texts of potentially relevant articles were examined by three researchers. Disagreements were resolved through discussion and reasons for exclusion were recorded.

## 2.2. Inclusion and Exclusion Criteria

We included studies with the following characteristics: (i) reported in English or Italian, based on co-author language abilities; (ii) cross-sectional, case–control or cohort studies; (iii) investigated HL using a validated tool; (iv) provided raw data, unadjusted or adjusted estimates of the association between HL and vaccination intention and/or status in any population(s). Any statistical analysis was considered eligible. According to Sorensen et al., we adopted the following HL definition: "[people's ability] to make judgements and take decisions in everyday life concerning healthcare, disease prevention and health promotion to maintain or improve their quality of life" [29]. Articles that analyzed HL with non-validated tools, investigated only specific HL (e.g., oral HL), focused on specific subdomains only, or in which data or estimates of the associations of interest were not retrievable were excluded.

#### 2.3. Data Collection and Quality Assessment

For each record included, three reviewers independently extracted the following information using a standardized data abstraction form: first author, year of publication, country, study design, main characteristics of the target population (age, ethnicity, recruitment process and number of participants), type of vaccine (e.g., against SARS-CoV-2, measles, etc.), tool used to assess HL, outcome definition and measurement, statistical analysis, main findings, and adjustment factors. Two main outcomes were distinguished: intention to vaccinate and vaccination status. Articles were then grouped according to the type of vaccine and a narrative synthesis was performed for each outcome. Three independent authors performed a quality assessment of the articles included using the Newcastle-Ottawa scale for cohort studies or its adapted version for cross-sectional studies [30] (Supplementary Table S2). Discrepancies were resolved by consensus. Articles were considered of high quality when the total score was  $\geq$ 7, fair quality if the score was  $\geq$ 5 and <7, and poor quality if the score was lower than 5.

# 3. Results

Overall, 3965 records were identified by database searching (Figure 1). After duplicate removal and screening by title and abstract, 95 articles were selected as eligible for full-text analysis, from which 74 were excluded with reasons, giving a total of 21 articles ultimately included in the systematic review. Of these, six articles investigated intention to vaccinate [31–36], 14 records explored vaccination status [37–50], and one study [51] combined the two outcomes in a single analysis. In this last example [51], the composite outcome resulted from three questions, two of which referred to the vaccinations received in the previous years. For the purposes of this review, therefore, we considered this study to be an investigation of vaccination status.

## 3.1. Characteristics of the Studies Included

## 3.1.1. Intention to Vaccinate

All studies investigating intention to vaccinate were published in 2021 and had a cross-sectional design (Table 1). Two were conducted in the United States [32,36], two in France [34,35], one in Japan [33] and one in Turkey [31]. In all studies but one [35], the authors specified the main characteristics of the target population: in one study, patients with chronic diseases were recruited from health clinics [32], while in three studies individuals were enrolled from educational settings (i.e., students or educators) [31,33,36], and in one study individuals attending homeless shelters were investigated [34]. About half the studies enrolled a large number of participants (i.e., more than 1000) [31,33,35]. All studies explored the intention to vaccinate against SARS-CoV-2. Quality was high in all cases except for one article [35], in which a lack of justification for the sample size and comparability between responders and non-responders were the main deficits (Supplementary Table S2).

## 3.1.2. Vaccination Status

The articles that investigated vaccination status were published from 2002 to 2020 (Table 2). The majority were conducted in the United States (n = 10) [37–39,41–45,47,48], two in Europe (Italy and Spain) [49,51], two in Asia (South Korea and Malaysia) [40,50] and one in Israel [46]. They mostly had a cross-sectional design (n = 10) [37,40,41,43,44,47–51], while three were cohort studies (prospective or retrospective) [38,39,42,45] and one was a casecontrol study [46]. The target populations were heterogeneous, comprising parents or caregivers (n = 4) [42,45,46,48], pregnant women (n = 1) [49], healthcare workers (n = 2) [40,51], the elderly (n = 3) [37,38,44], and patients with chronic conditions (n = 2) [39,41]. The remaining three studies recruited adults [43,47,50], in one case only women [47]. Data were obtained from people seeking medical care in six studies [39,42,45,47–49]. Ethnicity was specified in two cases [47,50]. Six studies enrolled more than 1000 individuals [37,38,41,43,44,47], one of which included more than 10,000 participants [43]. Seven articles considered a single vaccination [40,41,44,47,48,50,51], five investigated two vaccines or more [37–39,43,49], and in three cases the authors explored combined vaccinations [42,45,46]. As a result, influenza vaccination was the most investigated (n = 11) [37–41,43,44,47,49–51] followed by pneumococcal (n = 4) [37–39,43]. Other vaccines included were hexavalent [45], a combination of hexavalent, measles, mumps and rubella (MMR), and pneumococcal [42], and diphtheria, tetanus and pertussis (DTPa) together with hepatitis B (HBV) and MMR [46], HPV [48] and pertussis [49]. Quality was generally quite high apart from two cases [50,51] that lacked a sample size justification and evidence of comparability between responders and non-responders (Supplementary Table S2).





| First Author, Year       | Country | Study<br>Design | Target Population   | Vaccination | Study<br>Quality |
|--------------------------|---------|-----------------|---|-------------|------------------|
| Aslantekin-Özçoban, 2021 | Turkey  | CS              | Midwifery students (N = 1891)   | SARS-CoV-2  | 8                |
| Arvanitis, 2021          | USA     | CS              | Older adults with one or more chronic diseases<br>recruited from a community of<br>academic clinics (N = 601) | SARS-CoV-2  | 8                |
| Fukuda, 2021             | Japan   | CS              | School, college and university educators<br>aged 20–60 years (N = 1000)                                       | SARS-CoV-2  | 9                |
| Longchamps, 2021         | France  | CS              | Homeless people aged $\geq 18$ years recruited from short and long-term homeless shelters (N = 235)           | SARS-CoV-2  | 7                |
| Montagni, 2021           | France  | CS              | Adults >18 years from the general population<br>enrolled from PBS (N = 1647)                                  | SARS-CoV-2  | 6                |
| Patil, 2021              | USA     | CS              | College students (N = $256$ )   | SARS-CoV-2  | 8                |

CS: Cross-sectional. HL: Health Literacy. US: United States. PBS: population-based study.

| First Author, Year  | Country                 | Study Design  | Target Population  | Vaccination                           | Study<br>Quality |
|---|-------------------------|---|--|---------------------------------------|------------------|
| Scott, 2002   | US                      | Cross-sectional                                       | Community-dwelling Medicare aged<br>≥65 years enrolled in a national<br>managed care organization (N = 2722)                                 | Influenza,<br>pneumococcal            | 8                |
| Howard, 2006  | US                      | Retrospective<br>cohort                               | Community-dwelling Medicare aged $\geq 65$ years enrolled in a national managed care organization (N = 3260)                                 | Influenza,<br>pneumococcal            | 8                |
| White, 2008   | US                      | Cross-sectional                                       | Individuals aged $\geq 16$ years enrolled<br>from PBS (N = 18,100)   | Influenza,<br>pneumococcal            | 8                |
| Bennett, 2009   | US                      | Cross-sectional                                       | Individuals aged $\geq 65$ years enrolled<br>from PBS (N = 2668)   | Influenza                             | 9                |
| Pati, 2010  | US                      | Prospective<br>cohort                                 | Medicaid-eligible mothers recruited in<br>urban hospital (N = 506)   | Hexavalent                            | 9                |
| Amit Aharon, 2017   | Israel                  | Case-control  | Parents recruited from a health registry $(N = 731)$   | DTPa + HBV +<br>MMR                   | 7                |
| Moran, 2017   | US                      | Cross-sectional                                       | Hispanic women aged between 21 and<br>50 years recruited in clinics and<br>community sites (N = 1565)  | Influenza                             | 7                |
| Pati, 2017  | US                      | Prospective<br>cohort                                 | Medicaid-eligible mothers recruited in<br>urban hospital (N = 693)   | Hexavalent +<br>MMR +<br>pneumococcal | 8                |
| Widdice, 2018   | US                      | Cross-sectional                                       | Caregivers enrolled at time of the third<br>dose vaccination recruited in pediatric<br>adolescent and family medicine<br>practices (N = 422) | HPV                                   | 8                |
| Castro-Sánchez,<br>2018                                   | Spain                   | Cross-sectional                                       | Pregnant women recruited in<br>maternity wards (N = 119)   | Influenza,<br>pertussis               | 9                |
| Song, 2018  | South<br>Korea          | Cross-sectional                                       | Adult North Korean defectors (N = 399)   | Influenza                             | 6                |
| O'Conor, 2019   | US                      | Prospective   | Adults with COPD recruited in a community clinic ( $N = 388$ )   | Influenza,                            | 8                |
| Rafferty, 2019<br>Omar, 2020<br>Lorini, 2020 <sup>a</sup> | US<br>Malaysia<br>Italy | Cross-sectional<br>Cross-sectional<br>Cross-sectional | Adult diabetic patients (N = 4397)<br>Healthcare workers (N = 775)<br>Healthcare workers (N = 711)   | Influenza<br>Influenza<br>Influenza   | 8<br>10<br>6     |

|--|

<sup>a</sup> This study combined questions on vaccination status and intention in a single outcome. DPTa: diphtheria, tetanus, pertussis. HBV: hepatitis B. HPV: human papillomavirus. MMR: measles, mumps, rubella. PBS: population-based study. COPD: chronic obstructive pulmonary disease.

# 3.2. Association between HL and Vaccination Behavior

#### 3.2.1. Intention to Vaccinate

HL was assessed using self-reported comprehension items in all but one study [31,33–36], which used a tool with reading comprehension and numeracy items (i.e., Newest Vital Sign) [32]. The HL level was then used in the analysis as a mean score in two cases [31,33], was categorized into two classes in two studies [35,36] or into three classes in the remaining study [32] (Table 3). The intention to be vaccinated was generally explored with one question on attitude and willingness to receive the COVID-19 vaccine [33-36], and was expressed as a scale in half the studies [31–33] or as a categorization in the remaining three articles [34–36]. Accordingly, three studies performed multivariable linear regressions or ANOVA [31–33], while the other three used logistic regression or its extension [34–36]. Results were inconsistent: HL seemed not to influence the intention to be vaccinated in three cases [31,32,36], whereas a significant association was found in two articles [33,34], with low HL levels predicting vaccine hesitancy in one case [34] and higher HL associated with vaccination intention in the other [33]. Lastly, one study [35] recorded a significant association between poor HL and vaccination intention, but only when comparing vaccinehesitant and pro-vaccination individuals. All studies but one [32] conducted multivariable analyses; adjustment factors included were mainly socio-demographic characteristics.

| Author,                         | Н   | L   | Vaccination   | Intention  | Statistical                             | Main Ein Jinne   | Adjustment   |
|---------------------------------|---|---|---|--|---|--|--|
| Year                            | $\operatorname*{Measurement}_{\alpha}$                                      | Coding  | Measurement Coding  |  | Analysis                                | Main Findings  | Factors  |
| Aslantekin-<br>Özçoban,<br>2021 | HLS-EU-<br>Q25  | Continuous  | Nine questions<br>investigating trust,<br>perceived<br>effectiveness, and<br>benefits of the<br>COVID-19<br>vaccination   | Vaccination<br>attitude scale<br>(score: 0–5):<br>- low score:<br>negative attitude<br>- high score:<br>positive attitude                                    | Multivariable<br>linear<br>regression   | Non-significant<br>association<br>between HL and<br>vaccination attitude<br>( $a\beta = 0.027, p = 0.188$ )  | Attitudes<br>towards<br>COVID-19<br>vaccine;<br>perception of<br>COVID-19<br>causes  |
| Arvanitis,<br>2021              | NVS   | Three<br>categories:<br>- low<br>- marginal<br>- adequate   | Two questions:<br>- "I trust that any<br>future coronavirus<br>vaccine will be safe<br>and effective"<br>- "I will be vaccinated<br>for the coronavirus as<br>soon as a vaccine<br>becomes available" | Vaccination<br>agreement scale<br>(score: 0–10):<br>- low score:<br>no agreement<br>- high score:<br>total agreement   | ANOVA                                   | Non-significant<br>association between<br>HL and vaccination<br>agreement ( $p = 0.06$ )   | /  |
| Fukuda,<br>2021                 | HLS-EU-<br>Q47  | Continuous  | One question<br>relating to the<br>timing of<br>vaccination<br>intention after<br>inoculation<br>availability   | Vaccination<br>intention scale<br>(score: 1–5):<br>- low score:<br>will not inoculate<br>- high score:<br>immediately  | Multivariable<br>linear<br>regression   | Significant<br>association between<br>higher HL and<br>vaccination intention<br>(aβ = 0.021, p < 0.001)  | Gender; age;<br>academic<br>background;<br>being under<br>care of<br>physician   |
| Longchamps<br>2021              | " HLQ   | Two<br>categories:<br>- low<br>-<br>intermediate<br>or high | One question:<br>"If a vaccine<br>existed, would you be<br>willing to get<br>vaccinated?"   | Two categories<br>of vaccination<br>intention:<br>- yes: not hesitant<br>- no or<br>I don't know:<br>vaccine hesitant  | Multivariable<br>logistic<br>regression | Significant<br>association between<br>intermediate/high<br>HL and vaccine<br>hesitancy<br>(aOR = 0.38,<br>95% CI: 0.21–0.68)   | Gender; family<br>composition;<br>administrative<br>status   |
| Montagni,<br>2021               | 5-item scale<br>developed<br>by the<br>French<br>Public<br>Health<br>Agency | Two<br>categories:<br>- bad<br>- good                       | One question:<br>"Would you be<br>willing to get<br>vaccinated against<br>coronavirus even if<br>the vaccine<br>has not yet been fully<br>proven effective?"  | Three categories<br>of vaccination<br>intention:<br>- yes:<br>pro-vaccination<br>- I don't know:<br>vaccine hesitant<br>- no:<br>anti-vaccination            | Multinomial<br>logistic<br>regression   | - Significant<br>association between<br>poor HL and being<br>vaccine hesitant vs.<br>pro-vaccination<br>(aRRR = 1.44, 95% CI:<br>1.04–2.00)<br>- Non-significant<br>association between<br>poor HL and being<br>anti-vaccination<br>vs. pro-vaccination<br>(aRRR = 1.25,<br>95% CI: 0.96–1.63) | Gender; being<br>regularly<br>vaccinated<br>against the flu;<br>having an<br>up-to-date<br>vaccination;<br>studying or<br>working in the<br>health domain,<br>capacity to<br>detect fake<br>news |
| Patil, 2021                     | SILS  | Two<br>categories:<br>- low<br>- adequate                   | One question:<br>"How likely would<br>you be to get a<br>COVID-19 vaccine,<br>if available?"  | Two categories<br>of vaccination<br>intention:<br>- very likely:<br>willing to<br>undergo<br>vaccination<br>- somewhat or<br>not likely:<br>vaccine hesitant | Multivariable<br>logistic<br>regression | Non-significant<br>association<br>between low HL<br>and likelihood<br>to vaccinate<br>(aOR = 0.88,<br>95% CI: 0.50–1.56)   | Social network<br>size; gender;<br>race/ethnicity;<br>disability; first<br>generation<br>university<br>student status;<br>political<br>affiliation   |

# Table 3. Association between health literacy (HL) and vaccination intention against SARS-CoV-2.

a $\beta$ : adjusted beta coefficient. aOR: adjusted odds ratio. aRRR: adjusted relative risk ratio. ANOVA: analysis of variance. CI: confidence interval. COVID-19: coronavirus disease 2019.  $^{\alpha}$  HL tool: HLQ: Health literacy Questionnaire. HLS-EU-Q: European Health Literacy Survey Questionnaire. NVS: Newest Vital Sign. SILS: Single Item Literacy Screener.

# 3.2.2. Vaccination Status

Among studies investigating influenza vaccination, the instruments used to measure HL were heterogeneous, but mostly used reading or numeracy comprehension items [37–39,42–44,48–51] (Table 4). In just one case, the authors assessed HL using three different tools [49]. HL was categorized into two or three levels in approximately half the studies [37–39,41,47,50]. Influenza vaccine uptake was explored using one or more self-reported questions in all studies but one, in which the immunization status was extracted from a registry [49]. The vaccination uptake was evaluated variously in the previous year [39,41,43,44,50], in one or more specific periods [40,49,51], or across the whole life of the individual [37,38], whereas Lorini et al. used a combination of questions on vaccination status and intention to vaccinate [51]. Vaccination uptake was expressed as a binary variable in almost all studies [37-41,43,44,47,49,50]. Results were contrasting: after adjusting mostly for socio-demographic, health status and health habit factors, inadequate but not marginal HL was strongly associated with vaccination refusal in the samples analyzed by Scott et al. [37] and Howard et al. [38]; low HL levels seemed to positively influence vaccination uptake in people aged less than 40 years and negatively influence it among people older than 65 years in one case [43]; high HL levels were significantly associated with vaccine uptake in two studies [44,50], whereas no relationship between HL and immunization status was obtained in five analyses [39–41,47,51]. Lastly, the study that used different tools to investigate the outcome found a significant association between high HL levels and vaccination uptake in one case out of three [49], but the analyses were unadjusted.

As for pneumococcal vaccine, all but one study [43] used the short version of the Test of Functional Health Literacy in Adults (S-TOFHLA) as the HL assessment tool, which groups HL into two [39] or three categories [37,38]. The other article used the National Assessment of Adult Literacy questionnaire. All studies investigated vaccination status with a self-reported question, at least once in the entire life [37–39] or during the previous year [43]. The outcome was always dichotomized into yes or no, and all articles provided adjusted estimates, using either logistic [37–39] or probit regression models [43]. No significant relationship was reported between HL and vaccination status except in one case [37] in which inadequate HL was associated with no vaccination uptake. Adjustment factors comprised mainly socio-demographic variables and health conditions.

HPV vaccination status among girls was assessed in one study [48] in which the authors used the Rapid Estimate of Adult Literacy in Medicine to categorize parents' or caregivers' HL levels into three classes. The outcome was calculated as time to completion of three out of four vaccine doses and was divided into four categories in relation to the delay in completion: not delayed (≤12 months), delayed 12–24 months, delayed 24–36 months and delayed >36 months. A multinomial logistic regression analysis found no association between any HL level and the delay in completion of HPV doses for any of the interval times considered. The analysis was adjusted mainly for socio-demographic characteristics of caregivers and the target population.

The current vaccination status of children for hexavalent vaccination was investigated by Pati et al. [45], who used S-TOFHLA to classify the HL of mothers as 'adequate' or 'inadequate or marginal', whereas data on vaccination status were extracted from an immunization registry. After adjustment mainly for the mothers' socio-demographic variables, HL did not seem to predict the decision of mothers to vaccinate their children at three or seven months, according to multivariable logistic regression models.

Likewise, when exploring a similar population using the same HL tool several years later, but investigating the combination of hexavalent vaccine, MMR and pneumococcal vaccine, Pati et al. [42] did not find any relationship between maternal HL levels and the up-to-date immunization status of their children at 24 months, according to a univariable analysis.

The combined DTPa, MMR and HBV vaccination status was considered by Amit Aharon [46] using the Vaccine Health Literacy Scale to assess parents' HL, calculating its level as a continuous variable. With immunization data extracted from a registry, the authors performed a path analysis and found a direct effect between parents' communicative HL and the completion of the childhood vaccination protocol by the age of two, as well as an indirect effect between functional and critical HL and the same vaccination protocol.

| AA              | HL<br>Measurement <sup>α</sup> Coding |  | Vaccinati  | Vaccination Status<br>Measurement Coding                        |   |   |  |
|-----------------|---------------------------------------|--|--|---|---|---|--|
| Author,<br>Year |                                       |  | Measurement  |   |   | Main Findings   | Adjustment<br>Factors <sup>β</sup>   |
|                 |                                       |  |  | Influenz  | za  |   |  |
| Scott, 2002     | S-TOFHLA                              | Three<br>categories:<br>- inadequate<br>- marginal<br>- adequate | One SR<br>question:<br>having ever<br>received the<br>vaccination                    | Two<br>categories of<br>vaccination<br>status:<br>- yes<br>- no | Multivariable<br>logistic<br>regression                   | - Significant association between<br>inadequate HL and no vaccination<br>uptake (aOR = 1.4, 95% CI: 1.1–1.9)<br>- Non-significant association<br>between marginal HL and<br>no vaccination uptake<br>(aOR = 1.0, 95% CI: 0.7–1.4)   | AGR, education, income,<br>physician visit (last 3<br>months), MMSE, chronic<br>condition, IADL limitation |
| Howard,<br>2006 | S-TOHFLA                              | Three<br>categories:<br>- inadequate<br>- marginal<br>- adequate | One SR<br>question:<br>having ever<br>received the<br>vaccination                    | Two<br>categories of<br>vaccination<br>status:<br>- yes<br>- no | Multivariable<br>logistic<br>regression                   | <ul> <li>Significant association between<br/>inadequate HL and vaccination<br/>uptake (aOR = 0.76, p = 0.020)</li> <li>Non-significant association between<br/>marginal HL and vaccination uptake<br/>(aOR = 1.06, p = 0.707)</li> </ul>  | AGR, education, income,<br>tobacco consumption,<br>chronic conditions, area of<br>residence                |
| White, 2008     | NAAL                                  | Continuous   | One SR<br>question:<br>having<br>received the<br>vaccination in the<br>previous year | Two<br>categories of<br>vaccination<br>status:<br>- yes<br>- no | Marginal<br>maximum<br>likelihood<br>probit<br>regression | - Adults aged <40 years: significant<br>association between higher HL and<br>vaccination uptake<br>$(a\beta = -0.07, p < 0.05)$<br>- Adults aged 40–64 years:<br>non-significant association between<br>higher HL and vaccination uptake<br>$(a\beta = 0.01, p > 0.05)$<br>- Adults aged >65 years: significant<br>association between higher HL and<br>vaccination uptake<br>$(a\beta = 0.17, p < 0.05)$ | AGR, health status,<br>poverty level, insurance<br>coverage, oral reading<br>fluency                       |

**Table 4.** Association between health literacy (HL) and vaccination status by vaccine type.

| Author,                     | HI                      |   | Vaccina  | Vaccination Status   |   | Main Tindinga  | Adjustment  |
|-----------------------------|-------------------------|---|--|--|---|--|---|
| Year                        | Measurement $^{\alpha}$ | Coding  | Measurement  | Coding   | Analysis  | Main Findings  | Factors <sup>β</sup>  |
|                             |                         |   |  | Influenza  |   |  |   |
| Bennett,<br>2009            | NAAL                    | Continuous  | One SR<br>question:<br>having ever<br>received the<br>vaccination                            | Two<br>categories of<br>vaccination<br>status:<br>- yes<br>- no  | Marginal<br>maximum<br>likelihood<br>probit<br>regression | Significant association between higher<br>HL and vaccination uptake<br>$(a\beta = 0.14, p < 0.05)$   | AGR, education, income,<br>US born  |
| Moran, 2017                 | SBSQ                    | Two<br>categories:<br>- inadequate<br>- adequate          | One SR<br>question:<br>frequency of<br>vaccination<br>against<br>influenza                   | Two categories of<br>frequency of<br>vaccination:<br>- almost always or<br>always: regularly<br>receiving vaccination<br>- never, rarely, or<br>sometimes: not<br>regularly receiving<br>vaccination | Multivariable<br>logistic<br>regression                   | Non-significant association between<br>adequate HL and regularly<br>receiving influenza vaccination<br>(aOR = 1.12, 95% CI: 0.88–1.43)   | Country of birth,<br>educational level, annual<br>income, age, health<br>insurance, health state,<br>fatalism, acculturation,<br>years lived in the US,<br>religiosity, confidence in<br>the vaccine safety |
| Castro-<br>Sánchez,<br>2018 | SAHLSA-50               | Continuous  | Immunization<br>status<br>extracted from<br>the<br>vaccination<br>registry                   | Two categories of vaccination status:  | Mann–Whitney<br>U test                                    | Significant association between higher<br>HL and vaccination uptake<br>(p = 0.019)   |   |
|                             | NVS                     | Continuous  |  | vaccination during<br>pregnancy<br>- did not receive the   | Mann–Whitney<br>U test                                    | Non-significant association between<br>higher HL and vaccination uptake<br>(p = 0.320)   | /   |
|                             | SILS                    | Continuous  |  | vaccination during<br>pregnancy  | Mann–Whitney<br>U test                                    | Non-significant association between<br>higher HL and vaccination uptake<br>(p = 0.942)   |   |
| Song, 2018                  | S-KHLS                  | Three<br>categories:<br>- low<br>- intermediate<br>- high | One SR<br>question:<br>having<br>received the<br>vaccination in the<br>previous two<br>years | Two categories of<br>vaccination status:<br>- yes<br>- no  | Multivariable<br>logistic<br>regression                   | <ul> <li>Significant association between<br/>intermediate HL and<br/>vaccination uptake<br/>(aOR = 2.44, 95% CI: 1.19–5.00)</li> <li>Significant association between high<br/>HL and vaccination uptake<br/>(aOR = 2.10, 95% CI: 1.02–4.35)</li> </ul> | Age, gender, marital status,<br>duration of stay in other<br>countries before entry,<br>duration of stay in the<br>Republic of Korea  |

| Author,           | HL                      |   | Vaccination Status   |  | Statistical                               | Main Findings   | Adjustment   |
|-------------------|-------------------------|---|--|--|---|---|--|
| Year              | Measurement $^{\alpha}$ | Coding  | Measurement  | Coding   | Analysis                                  | Main Findings   | Factors <sup>β</sup>   |
|                   |                         |   |  | Influenza  |   |   |  |
| O'Conor,<br>2019  | S-TOFHLA                | Two<br>categories:<br>- limited<br>- adequate | One SR question:<br>having received<br>the vaccination in<br>the previous year   | Two categories of<br>vaccination status:<br>- yes<br>- no  | GEE model for<br>repeated<br>measurements | Non-significant association between<br>adequate HL and<br>vaccination uptake<br>(aOR =0.85, 95% CI: 0.62–1.18)  | AGR, income, number of<br>comorbidities, severity of<br>COPD   |
| Rafferty,<br>2019 | BRFSS                   | Two<br>categories:<br>- not low- low          | One SR question:<br>having received<br>the vaccination in<br>the previous year   | Two categories of<br>vaccination status:<br>- yes<br>- no  | Multivariable<br>logistic<br>regression   | Non-significant association between<br>low HL and vaccination uptake<br>(aOR = 0.98, 95% CI: 0.74–1.29)   | AGR, education,<br>household income, health<br>status  |
| Omar, 2020        | FCCHL                   | Continuous                                    | One SR<br>question:<br>"Did you have an<br>influenza<br>vaccination<br>between<br>November 2016<br>and October<br>2017?"                           | Two categories of<br>vaccination status:<br>- yes<br>- no  | Multivariable<br>logistic<br>regression   | Non-significant association between<br>higher HL and vaccination uptake:<br>- functional HL:<br>aOR = 1.04, 95% CI: 0.79–1.37<br>- critical HL:<br>aOR = 1.08, 95% CI: 0.76–1.53<br>- communicative HL:<br>aOR = 0.98, 95% CI: 0.65–1.45  | AGR, religion, education,<br>job category, department,<br>income, chronic disease,<br>marital<br>status, smoking status, and<br>living with person at high<br>risk of getting influenza<br>complications, knowledge,<br>behavioral, HL variables |
| Lorini, 2020      | IMETER                  | Continuous                                    | Three SR<br>questions:<br>having<br>received the<br>vaccination in<br>2016–2017, in<br>2017–2018, and<br>intention to<br>vaccinate in<br>2018–2019 | Three categories of<br>vaccination behavior:<br>- always get<br>vaccinated<br>- vaccinated at least<br>once in the previous<br>years or intended to<br>vaccinate (sometimes)<br>- never vaccinated<br>and did not intend to<br>vaccinate (never) | Multinomial<br>logistic<br>regression     | <ul> <li>Non-significant association<br/>between higher HL and<br/>vaccination behavior<br/>(sometimes vs. never:<br/>aRRR = 0.99, 95% CI: 0.97-1-01)</li> <li>Non-significant association<br/>between higher HL and<br/>vaccination behavior<br/>(always vs. never:<br/>aRRR = 0.98, 95% CI: 0.95–1.01)</li> </ul> | Gender, age,<br>mother language  |

| Author,          | HL                      |  | Vaccination Status  |   | Statistical   | Main Eindings  | Adjustment   |
|------------------|-------------------------|--|---|---|---|--|--|
| Year             | Measurement $^{\alpha}$ | Coding   | Measurement   | Coding  | Analysis  | Main Findings  | Factors <sup>β</sup>   |
|                  |                         |  |   | Pneumococ   | cal   |  |  |
| Scott, 2002      | S-TOFHLA                | Three<br>categories:<br>- inadequate<br>- marginal<br>- adequate | One SR<br>question:<br>having ever<br>received the<br>vaccination                       | Two categories of<br>vaccination status:<br>- yes<br>- no | Multivariable<br>logistic<br>regression                   | - Significant association between<br>inadequate HL and no<br>vaccination uptake<br>(aOR = 1.3, 95% CI: 1.1–1.7)<br>- Non-significant association<br>between marginal HL and no<br>vaccination uptake<br>(aOR = 1.2, 95% CI: 0.9–1.7)                 | AGR, education, income,<br>physician visit (last 3<br>months), MMSE, chronic<br>condition, IADL limitation |
| Howard,<br>2006  | S-TOFHLA                | Three<br>categories:<br>- inadequate<br>- marginal<br>- adequate | One SR<br>question:<br>having ever<br>received the<br>vaccination                       | Two categories of<br>vaccination status:<br>- yes<br>- no | Multivariable<br>logistic<br>regression                   | <ul> <li>Non-significant association between<br/>inadequate HL and<br/>vaccination uptake<br/>(aOR = 0.85, p = 0.114)</li> <li>Non-significant association between<br/>marginal HL and<br/>vaccination uptake<br/>(aOR = 0.91, p = 0.445)</li> </ul> | AGR, education, income,<br>tobacco consumption,<br>chronic conditions, area of<br>residence                |
| White, 2008      | NAAL                    | Continuous   | One SR<br>question:<br>having<br>received the<br>vaccination<br>in the<br>previous year | Two categories of<br>vaccination status:<br>- yes<br>- no | Marginal<br>maximum<br>likelihood<br>probit<br>regression | Non-significant association<br>between higher HL and<br>vaccination uptake<br>$(a\beta = -0.01, p > 0.05)$   | AGR, health status,<br>poverty level, insurance<br>coverage, oral reading<br>fluency                       |
| O'Conor,<br>2019 | S-TOFHLA                | Two<br>categories:<br>- limited<br>- adequate                    | One SR<br>question:<br>having ever<br>received the<br>vaccination                       | Two categories of<br>vaccination status:<br>- yes<br>- no | GEE<br>models for<br>repeated<br>measurements             | Non-significant association between<br>adequate HL and<br>vaccination uptake<br>(aOR = 1.01, 95% CI: 0.64–1.60)  | AGR, income, number of<br>comorbidities, severity of<br>COPD   |

| Author,          | Н                       | L  | Vaccination Status   |  | Statistical                             | Main Findings   | Adjustment   |
|------------------|-------------------------|--|--|--|---|---|--|
| Year             | Measurement $^{\alpha}$ | Coding   | Measurement  | Coding   | Analysis                                | Main Thomgs   | Factors <sup>β</sup>   |
|                  |                         |  |  | HPV  |   |   |  |
| Widdice,<br>2018 | REALM                   | Three<br>categories of<br>HL grade<br>equivalent:<br>- 6th grade<br>or below<br>(very low)<br>- 7th to 8th<br>grade (low)<br>- high school | One SR<br>question:<br>time to<br>completion of<br>three doses<br>(days<br>between<br>the first and<br>third dose) | Four categories of<br>time to<br>completion of<br>vaccination cycle:<br>- not delayed<br>(≤12 months)<br>- delayed<br>(12–24 months)<br>- delayed<br>(24–36 months)<br>- delayed<br>(>36 months) | Multinomial<br>logistic<br>regression   | <ul> <li>Non-significant association<br/>between very low HL and<br/>delayed completion of<br/>vaccination cycle</li> <li>Non-significant association<br/>between low HL and<br/>delayed completion of<br/>vaccination cycle</li> </ul> | Race, caregiver education,<br>adolescent insurance, gap<br>in adolescent insurance<br>since HPV dose, number of<br>parents in household,<br>parents' marital status,<br>adolescent health visits in<br>the previous year,<br>appointment availability,<br>caregiver ability to obtain<br>timely appointments for<br>adolescent's medical care,<br>ability to get through on the<br>telephone |
|                  |                         |  |  | Hexavaler  | ıt                                      |   |  |
| Pati, 2010       | S-TOFHLA                | Two<br>categories:<br>- inadequate or<br>marginal<br>- adequate  | Immunization<br>status<br>extracted from<br>vaccination<br>registry  | Two categories for<br>up-to-date<br>vaccination<br>status<br>at 3 and 7 months:<br>- yes<br>- no   | Multivariable<br>logistic<br>regression | Non-significant association<br>between higher maternal HL<br>and child's up-to-date<br>immunization status:<br>- 3 months (aOR = 1.08, 95% CI:<br>0.67–1.76)<br>- 7 months (aOR = 0.92, 95% CI:<br>0.57–1.48)                           | Maternal race/ethnicity,<br>age, education, receiving<br>antenatal care, participation<br>in WIC program, marital<br>status, location of the<br>infant's health care facility,<br>vaccination status at the age<br>of 3 months (for 7 months<br>model only)  |

| Author.                     | H                       | Ĺ   | Vaccination Status  |  | Statistical            |   | Adjustment           |
|-----------------------------|-------------------------|---|---|--|------------------------|---|----------------------|
| Year                        | Measurement $^{\alpha}$ | Coding  | Measurement   | Coding   | Analysis               | Main Findings   | Factors <sup>β</sup> |
|                             |                         |   |   | Hexavalent + MMR + I   | Pneumococcal           |   |                      |
| Pati, 2017                  | S-TOFHLA                | Two<br>categories:<br>- inadequate or<br>marginal<br>- adequate | Immunization<br>status<br>extracted from<br>vaccination<br>registry | Two categories for<br>up-to-date<br>vaccination status at<br>24 months:<br>- yes<br>- no | Chi-square<br>test     | Non-significant association between<br>maternal HL and child's up-to-date<br>immunization status at 24 months   | /                    |
|                             |                         |   |   | DTPa + MMR -   | + HBV                  |   |                      |
| Amit<br>Aharon,<br>2017     | VHLS                    | Continuous  | Immunization<br>status<br>extracted from<br>vaccination<br>registry | Completion of<br>vaccination<br>protocol<br>at 2 years:<br>- yes<br>- no                 | Path<br>analysis       | <ul> <li>Significant association between<br/>higher communicative HL and<br/>completion of vaccination protocol at<br/>2 years (β = 0.06, p &lt; 0.05)</li> <li>Functional HL and critical HL had<br/>an indirect effect, mediated through<br/>other variables, on completion of the<br/>vaccination protocol at 2 years</li> </ul> | NA                   |
|                             |                         |   |   | Pertussis  | ,                      |   |                      |
| Castro-<br>Sánchez,<br>2018 | SAHLSA-50               | Continuous  | Immunization<br>status  | Two categories of vaccination status:  | Mann–Whitney<br>U test | Significant association between higher<br>HL and vaccination uptake<br>(p < 0.05)   | /                    |
|                             | NVS                     | Continuous  | vaccination<br>registry   | rrom - received the<br>ton vaccination<br>y during pregnancy<br>- did not receive the    | Mann–Whitney<br>U test | Non-significant association between<br>higher HL and vaccination uptake<br>(p > 0.05)   | ,                    |
|                             | SILS                    | Continuous  |   | vaccination during pregnancy   | Mann–Whitney<br>U test | Non-significant association between<br>higher HL and vaccination uptake<br>(p > 0.05)   |                      |

a $\beta$ : adjusted beta coefficient. aOR: adjusted odds ratio. aRRR: adjusted relative risk ratio. CI: confidence interval. GEE: generalized estimating equation. DPTa: diphtheria, tetanus, pertussis. HBV: hepatitis B. HPV: human papillomavirus. MMR: measles, mumps, rubella. SR: self-reported.  $^{\alpha}$  HL tool: TOFHLA: Test of Functional Health Literacy in Adults. NAAL: National Assessment of Adult Literacy. VHLS: Vaccine Health Literacy Scale. SBSQ: Set of Brief Screening Questions. REALM: Rapid Estimate of Adult Literacy in Medicine. SAHLSA: Short Assessment of Health Literacy for Spanish Adults. NVS: Newest Vital Sign. FCCHL: Functional Communicative Critical Health Literacy. IMETER: Italian Medical Term Recognition Test. BRFSS: Behavioral Risk Factor Surveillance System. S-KHLS: Korean Health Literacy Scale.  $^{\beta}$  Adjustment factors: AGR: Age, gender, race. COPD: Chronic obstructive pulmonary disease. MMSE: Mini Mental State Examination. IADL: Instrumental activities of daily living. WIC: Women, Infants, and Children.

Lastly, none of the three HL tools used by Castro-Sanchez et al. [49] detected any difference in the mean HL value of new mothers and pertussis vaccination received during pregnancy, according to a univariable analysis.

# 4. Discussion

The COVID-19 pandemic has rekindled interest in the importance of the population's adherence to immunization programs and, consequently, the need to identify factors associated with vaccination uptake [52]. Among such factors, we investigated HL, which is broadly considered a social determinant of health [21,53,54] and a driver of healthy behavior [22,55], but we did not find conclusive evidence of its influence on the vaccination decision-making process. Because vaccination intention does not always reflect real behavior, and predictors might differ between the two aspects [56,57], we distinguished intention to vaccinate from vaccination status. However, in line with the mixed evidence provided by a previous review [23], our findings were largely inconsistent for both outcomes, probably due to the high degree of heterogeneity in the methods used. The issue of the multitude of tools commonly used to quantify HL [58], and accordingly the different domains explored [59], is widely discussed in the literature. In our review, we also found that different tools were used by researchers, and only some measured the individual's capacity to read and understand actual material, minimizing the risk of an inaccurate self-assessment [17]. In this context, the development of a comprehensive instrument for HL evaluation is surely a challenge, but it would definitely enable a more precise estimation of the magnitude of the problem and a better comparison of evidence, even though HL remains strongly connected with cultural and social aspects that make it difficult to isolate this concept [17]. There are similar concerns about the measurement of outcomes, as recently demonstrated in a review that found different rates of vaccination acceptance according to the scale used to quantify COVID-19 vaccination intention [1]. The high degree of variability in the definition of vaccination status, which includes being up-to-date with vaccinations in the last few years, undergoing vaccination at least once over the individual's entire life, or delaying the completion of a vaccination cycle, was also a concern. In addition, the cross-sectional design adopted in most studies complicates the causal interpretation of the findings [23]. For these reasons, to help clarify the role of HL in the vaccination decision-making process, future research on the topic should devise a longitudinal approach with a standardized methodology for the definition and measurement of both exposure and outcomes [23].

Apart from these general methodological considerations, the studies we found on intention to vaccinate focused exclusively on COVID-19 vaccines, probably because researchers wanted to investigate perceptions and intentions regarding newly developed vaccines administered during an out-of-the-ordinary campaign [60]. Our results suggest that factors other than HL are likely to explain people's beliefs and intentions towards COVID-19 vaccines [31,32], such as trust in the government and institutions [32]. For this reason, communication strategies aimed at increasing public confidence in health authorities and helping people understand why recommended measures are useful to them and their community may be the most effective in promoting COVID-19 vaccine acceptance [61]. However, given the emergency context in which these surveys were conducted, more studies are needed to clarify the role of HL in the intention to vaccinate against SARS-CoV-2, but also against other diseases, particularly as, in the latter case, we were unable to find any relevant studies. In addition, to avoid polarizing the discussion around vaccines [60], future studies should differentiate between those who are hesitant and those who are openly against vaccination, as the determinants of the intention to vaccinate may be different in these two subgroups [62-64].

Besides the individual determinants that play a role in vaccination intention [65], a few factors may be critical in the actual administration of the injection [66], such as the availability and proximity of vaccination centers [66], the ease with which an appointment can be made [12], or the funding/reimbursement scheme [67]. In our review, the articles that investigated vaccination status mostly explored the determinants of influenza vaccination,

probably because it is broadly recommended for the general population, there is an annual immunization program that struggles to reaches the desired coverage threshold, and there are huge variations in the uptake rates according to age and ethnicity [68]. Notably, the fact that a weak but positive association between HL and influenza vaccination uptake was mostly found in individuals aged more than 65 years [37,38,43,44,50] may be explained by the increased vulnerability of this age group to severe influenza outcomes, a factor often mentioned in the routine promotion campaigns that may encourage literate individuals to adhere to the recommended vaccination program [69]. In addition, the annual publicity for influenza vaccination delivery programs may promote vaccination uptake, which is different to what happens for pneumococcal vaccination, where there are less-widespread campaigns and the population's perceived risk is particularly low [67]. As for the few studies focusing on pediatric and adolescent vaccinations, since we did not find consistent association between vaccination status and parents' HL [42,45,46,48], more studies should be undertaken to investigate what influences vaccination uptake, especially considering that vaccine hesitancy in parents has contributed to the recent increase in vaccine-preventable disease outbreaks registered worldwide over recent years [9,70,71]. Furthermore, given that poor communication with parents was likely responsible for the association between vaccination rejection and a high level of education [49], increased attention should be given to communication strategies targeted to this particular group [72]. Specifically, tailored instruments and informative content that takes into account opinions, feelings and gaps in knowledge of the different vaccinations should be devised [73].

This study has some strengths and limitations. Firstly, we included observational studies that provided a general assessment of HL or that investigated all aspects of HL, excluding articles that analyzed only specific sub-domains. Nevertheless, given that we included articles that measured HL through validated and widely implemented tools, the resulting HL estimates can be considered reliable in relation to the multifaceted nature of the concept. Secondly, since our focus was HL generally, we excluded articles that investigated specific HL (e.g., cancer literacy, oral literacy). The other limitations are mostly related to the primary studies included in this review. Heterogeneity in the coding and measurement of HL and outcomes was found, largely limiting the opportunity to provide a quantitative synthesis. In addition, since our results are mostly based on self-reported outcomes, social desirability bias could affect the accuracy of our conclusions. Furthermore, since most studies were from the United States, and several of them analyzed specific subgroups, further research should be conducted both at the regional and national level to improve the generalizability of the findings. Nevertheless, to the best of our knowledge, this is the first review to perform an up-to-date systematic collection of evidence on the topic, expanding the findings provided in a previous review [23]. As a result, we were able to include information on COVID-19 vaccination. In addition, we were able to synthesize evidence on two different aspects of the vaccination decision-making process, namely, intention to vaccinate and vaccination status.

## 5. Conclusions

This review summarizes the current evidence on HL and intention to vaccinate and vaccination status. Despite some weak but positive results for influenza vaccination uptake in individuals aged more than 65 years, the relationship between HL and vaccination behavior remains scarcely supported by evidence. Differences in the methods used may explain the inconsistencies we found. Further research using a standardized approach is needed to clarify the role of HL in the vaccination decision-making process.

**Supplementary Materials:** The following supporting information can be downloaded at: https: //www.mdpi.com/article/10.3390/vaccines10111832/s1, Table S1: Search strategies used in the systematic review; Table S2: Quality assessment of the articles included in the systematic review according to the Newcastle-Ottawa scale for cohort and case–control studies and its adapted version for cross-sectional studies. Author Contributions: Conceptualization, V.B.; methodology, L.M.S. and V.B.; formal analysis, L.M.S.; investigation, L.M.S., C.I., A.S. and M.R.D.B.; data curation, L.M.S., C.I., A.S. and M.R.D.B.; writing—original draft preparation, L.M.S. and C.I.; writing—review and editing, V.B. and G.M.; visualization, V.B., G.M., C.M., C.D.V. and P.V.; supervision, C.I. and V.B.; project administration, C.M., C.D.V. and P.V. All authors have read and agreed to the published version of the manuscript.

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