

Newcastle-Ottawa quality assessment scale (NOS)

Study 1

Selection

- Is the case definition adequate?
a) Yes, with independent validation. *1 score*
- Representativeness of the cases
a) Consecutive or obviously representative series of cases. *
- Selection of Controls
a) Community controls. *1 score*
- Definition of Controls
a) No history of disease (endpoint). *1 score*

2. Comparability

- Comparability of cases and controls on the basis of design or analysis
a) Study controls for lymph node involvement, tumor grade. * b) Study controls for additional factors (e.g., age, HPV status). *

3. Exposure

- Ascertainment of exposure
a) Secure record (e.g., surgical records). *1 score*
- Same method of ascertainment for cases and controls
a) Yes. *1 score*
- Non-Response rate
a) Same rate for both groups. *1 score*

Study 2

1. Selection

- Is the case definition adequate?
a) Yes, with independent validation. *1 score*
- Representativeness of the cases
a) Consecutive or obviously representative series of cases. *
- Selection of Controls
a) Community controls. *1 score*
- Definition of Controls
a) No history of disease (endpoint). *1 score*

2. Comparability

- Comparability of cases and controls on the basis of design or analysis
a) Study controls for lymph node involvement, tumor grade. *

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- b) Study controls for additional factors (e.g., age, sex). *

3. Exposure

- Ascertainment of exposure
 - a) Secure record (e.g., surgical records). *1 score*
- Same method of ascertainment for cases and controls
 - a) Yes. *1 score*
- Non-Response rate
 - a) Same rate for both groups. *1 score*

Study 3

1. Selection

- Is the case definition adequate?
 - a) Yes, with independent validation. *1 score*
- Representativeness of the cases
 - a) Consecutive or obviously representative series of cases. *
- Selection of Controls
 - a) Community controls. *1 score*
- Definition of Controls
 - a) No history of disease (endpoint). *1 score*

2. Comparability

- Comparability of cases and controls on the basis of design or analysis
 - a) Study controls for lymph node involvement, tumor grade. *
 - b) Study controls for additional factors (e.g., TNM stage). *

3. Exposure

- Ascertainment of exposure
 - a) Secure record (e.g., surgical records). *1 score*
- Same method of ascertainment for cases and controls
 - a) Yes. *1 score*
- Non-Response rate
 - a) Same rate for both groups. *1 score*

Study 4

1. Selection

- Is the case definition adequate?
 - a) Yes, with independent validation. *1 score*

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- Representativeness of the cases
 - a) Consecutive or obviously representative series of cases. *
- Selection of Controls
 - a) Community controls. *1 score*
- Definition of Controls
 - a) No history of disease (endpoint). *1 score*

2. Comparability

- Comparability of cases and controls on the basis of design or analysis
 - a) Study controls for lymph node involvement, tumor grade. *
 - b) Study controls for additional factors. *

3. Exposure

- Ascertainment of exposure
 - a) Secure record (e.g., surgical records). *1 score*
- Same method of ascertainment for cases and controls
 - a) Yes. *1 score*
- Non-Response rate
 - a) Same rate for both groups. *1 score*

Study 5

1. Selection

- Is the case definition adequate?
 - a) Yes, with independent validation. *1 score*
- Representativeness of the cases
 - a) Consecutive or obviously representative series of cases. *
- Selection of Controls
 - a) Community controls. *1 score*
- Definition of Controls
 - a) No history of disease (endpoint). *1 score*

2. Comparability

- Comparability of cases and controls on the basis of design or analysis
 - a) Study controls for lymph node involvement, tumor grade. *
 - b) Study controls for additional factors (e.g., patient-specific factors). *

3. Exposure

- Ascertainment of exposure
 - a) Secure record (e.g., surgical records). *1 score*

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- Same method of ascertainment for cases and controls
a) Yes. *1 score*
- Non-Response rate
a) Same rate for both groups. *1 score*

Study 6

1. Selection

- Is the case definition adequate?
a) Yes, with independent validation. *1 score*
- Representativeness of the cases
a) Consecutive or obviously representative series of cases. *
- Selection of Controls
a) Community controls. *1 score*
- Definition of Controls
a) No history of disease (endpoint). *1 score*

2. Comparability

- Comparability of cases and controls on the basis of design or analysis
a) Study controls for lymph node involvement, tumor grade. * b) Study controls for additional factors (e.g., matched patient design). *

3. Exposure

- Ascertainment of exposure
a) Secure record (e.g., surgical records). *1 score*
- Same method of ascertainment for cases and controls
a) Yes. *1 score*
- Non-Response rate
a) Same rate for both groups. *1 score*

Study 7

Selection

- Is the case definition adequate?
a) Yes, with independent validation. *1 score*
- Representativeness of the cases
a) Consecutive or obviously representative series of cases. *
- Selection of Controls
a) Community controls. *1 score*
- Definition of Controls
a) No history of disease (endpoint). *1 score*

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2. Comparability

- Comparability of cases and controls on the basis of design or analysis
 - a) Study controls for lymph node involvement, tumor grade. * b) Study controls for additional factors (e.g., HPV status). *

3. Exposure

- Ascertainment of exposure
 - a) Secure record (e.g., surgical records). *1 score*
- Same method of ascertainment for cases and controls
 - a) Yes. *1 score*
- Non-Response rate
 - a) Same rate for both groups. *1 score*

Study 8

Selection (Maximum 4 Stars):

1. Representativeness of the Exposed Cohort: ★★

- The study includes a large and diverse cohort of HPV+ oropharyngeal squamous cell carcinoma (OPSCC) patients. This represents a well-defined patient population.

2. Selection of the Non-Exposed Cohort: ★★

- The study compares patients with high versus low intratumoral CD103+ immune cell abundance, allowing a comparison within the same patient population based on immune cell profiles.

3. Ascertainment of Exposure: ★★

- CD103+ cell abundance was measured using immunohistochemistry, a validated and standardized method.

4. Demonstration That Outcome of Interest Was Not Present at Start of Study: ★

- The study focuses on the abundance of CD103+ immune cells at diagnosis before treatment, ensuring that the outcome (survival) is not influenced by prior treatments.

Total Selection Score: 4/4 Stars

Comparability (Maximum 2 Stars):

1. Comparability of Cohorts on the Basis of the Design or Analysis: ★★

- The study controls for significant confounders such as stage, age, and smoking status using multivariable analysis, making the comparisons reliable.

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Total Comparability Score: 2/2 Stars

Outcome (Maximum 3 Stars):

1. **Assessment of Outcome: ★★**
 - Overall survival (OS) and progression-free survival (PFS) were measured using consistent statistical methods such as Kaplan-Meier analysis and multivariable Cox proportional hazard models.
2. **Was Follow-Up Long Enough for Outcomes to Occur?: ★**
 - The study had a median follow-up period of over 5 years, which is sufficient to observe survival outcomes in this patient population.
3. **Adequacy of Follow-Up of Cohorts: ★**
 - The study followed patients through the treatment period, although being retrospective may pose a limitation in long-term consistency.

Total Outcome Score: 3/3 Stars

Total NOS Score:

- **Selection:** 4/4
- **Comparability:** 2/2
- **Outcome:** 3/3
- **Overall NOS Score:** 9/9 Stars

Study 9

1. **Selection**
 - Is the case definition adequate?
 - a) Yes, with independent validation. *1 score*
 - Representativeness of the cases
 - a) Consecutive or obviously representative series of cases. *
 - Selection of Controls
 - a) Community controls. *1 score*
 - Definition of Controls
 - a) No history of disease (endpoint). *1 score*
2. **Comparability**
 - Comparability of cases and controls on the basis of design or analysis
 - a) Study controls for lymph node involvement, tumor grade. * b) Study controls for additional factors (e.g., tumor grade, age). *

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3. Exposure

- Ascertainment of exposure
 - a) Secure record (e.g., surgical records). *1 score*
- Same method of ascertainment for cases and controls
 - a) Yes. *1 score*
- Non-Response rate
 - a) Same rate for both groups. *1 score*

Study 10

1. Selection

- Is the case definition adequate?
 - a) Yes, with independent validation. *1 score*
- Representativeness of the cases
 - a) Consecutive or obviously representative series of cases. *
- Selection of Controls
 - a) Community controls. *1 score*
- Definition of Controls
 - a) No history of disease (endpoint). *1 score*

2. Comparability

- Comparability of cases and controls on the basis of design or analysis
 - a) Study controls for lymph node involvement, tumor grade. * b) Study controls for additional factors (e.g., HPV status, tumor stage). *

3. Exposure

- Ascertainment of exposure
 - a) Secure record (e.g., surgical records). *1 score*
- Same method of ascertainment for cases and controls
 - a) Yes. *1 score*
- Non-Response rate
 - a) Same rate for both groups. *1 score*

Study 11;

Selection (Maximum 4 Stars):

1. Representativeness of the Exposed Cohort: ★

- The study uses data from The Cancer Genome Atlas (TCGA) and the Fred Hutchinson Cancer Research Center's Oralchip study, providing a representative sample of OSCC patients.

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2. Selection of the Non-Exposed Cohort: ★

- The study compares immune cell composition in HPV-positive and HPV-negative OSCC patients.

3. Ascertainment of Exposure: ★

- Exposure to immune phenotypes is determined through CIBERSORT analysis of gene expression profiles, a validated computational method.

4. Demonstration That Outcome of Interest Was Not Present at Start of Study: ★

- The study focuses on immune cell abundance before survival outcomes, ensuring initial independence.

Total Selection Score: 4/4 Stars

Comparability (Maximum 2 Stars):

1. Comparability of Cohorts on the Basis of the Design or Analysis: ★★

- The study controls for key confounders like age, HPV status, tumor stage, and smoking history through multivariable Cox regression.

Total Comparability Score: 2/2 Stars

Outcome (Maximum 3 Stars):

1. Assessment of Outcome: ★

- The study uses multivariable Cox regression analysis for survival, focusing on overall survival (OS) as the primary outcome.

2. Was Follow-Up Long Enough for Outcomes to Occur?: ★★

- The follow-up period spans up to 5,480 days (approx. 15 years), which is sufficient for observing survival outcomes in OSCC patients.

3. Adequacy of Follow-Up of Cohorts: ★

- The study reports follow-up information for most patients, but some data (e.g., smoking history) is missing for a subset.

Total Outcome Score: 3/3 Stars

Total NOS Score:

- **Selection: 4/4**
- **Comparability: 2/2**
- **Outcome: 3/3**
- **Overall NOS Score: 9/9 Stars**

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Author	Study	Selection (4 Stars)	Comparability (2 Stars)	Outcome (3 Stars)	Total NOS Score
Muijlwijk, 2024 (38)	Study 1	4	2	3	9/9
Oliveira, 2023 (39)	Study 2	4	2	3	9/9
Ida, 2021 (40)	Study 3	4	2	3	9/9
Chen, 2021 (41)	Study 4	4	1	3	8/9
Kortekaas, 2020 (42)	Study 5	4	2	3	9/9
Mazzoni, 2020 (43)	Study 6	3	2	3	8/9
Hewavisenti, 2020 (44)	Study 7	4	2	3	9/9
Solomon, 2019 (45)	Study 8	4	2	3	9/9
Xiao, 2019 (46)	Study 9	4	2	3	9/9
Duhen, 2018 (47)	Study 10	4	2	3	9/9
Vora, 2017 (48)	Study 11	4	2	3	9/9