NIH Quality Assessment of Case-Control Studies
Aqueous Humor Markers in Retinoblastoma, a Review

Benjamin K. Ghiam, Liya Xu, PhD, Jesse L. Berry, MD

1. Study: **Dias et al. 1971**

Criteria	Yes	No	Other (CD, NR, NA)*
1. Was the research question or objective in this paper clearly stated and appropriate?	Yes		
2. Was the study population clearly specified and defined?	Yes		
3. Did the authors include a sample size justification?	Yes		
4. Were controls selected or recruited from the same or similar population that gave rise to the cases (including the same timeframe)?	Yes		
5. Were the definitions, inclusion and exclusion criteria, algorithms or processes used to identify or select cases and controls valid, reliable, and implemented consistently across all study participants?	Yes		
6. Were the cases clearly defined and differentiated from controls?	Yes		
7. If less than 100 percent of eligible cases and/or controls were selected for the study, were the cases and/or controls randomly selected from those eligible?			NA
8. Was there use of concurrent controls?	Yes		

Criteria	Yes	No	Other (CD, NR, NA)*
9. Were the investigators able to confirm that the exposure/risk occurred prior to the development of the condition or event that defined a participant as a case?	Yes		
10. Were the measures of exposure/risk clearly defined, valid, reliable, and implemented consistently (including the same time period) across all study participants?			NA
11. Were the assessors of exposure/risk blinded to the case or control status of participants?			CD
12. Were key potential confounding variables measured and adjusted statistically in the analyses? If matching was used, did the investigators account for matching during study analysis?		No	

Quality Rating (Good, Fair, or Poor): **Fair**
Comments: small n, statistical analysis of control group not performed, no p-value obtained
*CD, cannot determine; NA, not applicable; NR, not reported

2. Study: **Kabak and Romano 1975**

Criteria	Yes	No	Other (CD, NR, NA)*
1. Was the research question or objective in this paper clearly stated and appropriate?	Yes		
2. Was the study population clearly specified and defined?	Yes		

Criteria	Yes	No	Other (CD, NR, NA)*
3. Did the authors include a sample size justification?	Yes		
4. Were controls selected or recruited from the same or similar population that gave rise to the cases (including the same timeframe)?	Yes		
5. Were the definitions, inclusion and exclusion criteria, algorithms or processes used to identify or select cases and controls valid, reliable, and implemented consistently across all study participants?	Yes		
6. Were the cases clearly defined and differentiated from controls?	Yes		
7. If less than 100 percent of eligible cases and/or controls were selected for the study, were the cases and/or controls randomly selected from those eligible?			NA
8. Was there use of concurrent controls?	Yes		
9. Were the investigators able to confirm that the exposure/risk occurred prior to the development of the condition or event that defined a participant as a case?	Yes		
10. Were the measures of exposure/risk clearly defined, valid, reliable, and implemented consistently (including the same time period) across all study participants?			NA
11. Were the assessors of exposure/risk blinded to the case or control status of participants?			CD

Criteria	Yes	No	Other (CD, NR, NA)*
12. Were key potential confounding variables measured and adjusted statistically in the analyses? If matching was used, did the investigators account for matching during study analysis?		No	

Quality Rating (Good, Fair, or Poor): **Fair**

Comments: small n, statistical analysis against control group not performed no p-value obtained

*CD, cannot determine; NA, not applicable; NR, not reported

3. Study: **Piro et al. 1978**

Criteria	Yes	No	Other (CD, NR, NA)*
1. Was the research question or objective in this paper clearly stated and appropriate?	Yes		
2. Was the study population clearly specified and defined?	Yes		
3. Did the authors include a sample size justification?	Yes		
4. Were controls selected or recruited from the same or similar population that gave rise to the cases (including the same timeframe)?		No	
5. Were the definitions, inclusion and exclusion criteria, algorithms or processes used to identify or select cases and controls valid, reliable, and implemented consistently across all study participants?	Yes		
6. Were the cases clearly defined and differentiated from controls?	Yes		

Criteria	Yes	No	Other (CD, NR, NA)*
7. If less than 100 percent of eligible cases and/or controls were selected for the study, were the cases and/or controls randomly selected from those eligible?			NA
8. Was there use of concurrent controls?		no	
9. Were the investigators able to confirm that the exposure/risk occurred prior to the development of the condition or event that defined a participant as a case?	Yes		
10. Were the measures of exposure/risk clearly defined, valid, reliable, and implemented consistently (including the same time period) across all study participants?			NA
11. Were the assessors of exposure/risk blinded to the case or control status of participants?		no	
12. Were key potential confounding variables measured and adjusted statistically in the analyses? If matching was used, did the investigators account for matching during study analysis?		no	

Quality Rating (Good, Fair, or Poor): **Fair**

Comment: no control group was used in study, no statistics was performed

*CD, cannot determine; NA, not applicable; NR, not reported

4. Study: __Abramson et al. 1979__

Criteria	Yes	No	Other (CD, NR, NA)*

Criteria	Yes	No	Other (CD, NR, NA)*
1. Was the research question or objective in this paper clearly stated and appropriate?	yes		
2. Was the study population clearly specified and defined?	yes		
3. Did the authors include a sample size justification?	yes		
4. Were controls selected or recruited from the same or similar population that gave rise to the cases (including the same timeframe)?	yes		
5. Were the definitions, inclusion and exclusion criteria, algorithms or processes used to identify or select cases and controls valid, reliable, and implemented consistently across all study participants?	yes		
6. Were the cases clearly defined and differentiated from controls?	yes		
7. If less than 100 percent of eligible cases and/or controls were selected for the study, were the cases and/or controls randomly selected from those eligible?			NA
8. Was there use of concurrent controls?	yes		
9. Were the investigators able to confirm that the exposure/risk occurred prior to the development of the condition or event that defined a participant as a case?	yes		

Criteria	Yes	No	Other (CD, NR, NA)*
10. Were the measures of exposure/risk clearly defined, valid, reliable, and implemented consistently (including the same time period) across all study participants?			NA
11. Were the assessors of exposure/risk blinded to the case or control status of participants?		no	
12. Were key potential confounding variables measured and adjusted statistically in the analyses? If matching was used, did the investigators account for matching during study analysis?		no	

Quality Rating (Good, Fair, or Poor): **Good**

*CD, cannot determine; NA, not applicable; NR, not reported

5. Study: Dias 1979

Criteria	Yes	No	Other (CD, NR, NA)*
1. Was the research question or objective in this paper clearly stated and appropriate?	yes		
2. Was the study population clearly specified and defined?	yes		
3. Did the authors include a sample size justification?	yes		
4. Were controls selected or recruited from the same or similar		no	

Criteria	Yes	No	Other (CD, NR, NA)*
population that gave rise to the cases (including the same timeframe)?			
5. Were the definitions, inclusion and exclusion criteria, algorithms or processes used to identify or select cases and controls valid, reliable, and implemented consistently across all study participants?	yes		
6. Were the cases clearly defined and differentiated from controls?		no	
7. If less than 100 percent of eligible cases and/or controls were selected for the study, were the cases and/or controls randomly selected from those eligible?			NA
8. Was there use of concurrent controls?		no	
9. Were the investigators able to confirm that the exposure/risk occurred prior to the development of the condition or event that defined a participant as a case?	yes		
10. Were the measures of exposure/risk clearly defined, valid, reliable, and implemented consistently (including the same time period) across all study participants?		NA	
11. Were the assessors of exposure/risk blinded to the case or control status of participants?		no	
12. Were key potential confounding variables measured and adjusted statistically in the analyses? If matching was used, did the investigators account for matching during study analysis?		no	

Quality Rating (Good, Fair, or Poor): **Fair**
Comment: no controls used

*CD, cannot determine; NA, not applicable; NR, not reported

6. Study: Dias 1979'

Criteria	Yes	No	Other (CD, NR, NA)*
1. Was the research question or objective in this paper clearly stated and appropriate?	yes		
2. Was the study population clearly specified and defined?	yes		
3. Did the authors include a sample size justification?	yes		
4. Were controls selected or recruited from the same or similar population that gave rise to the cases (including the same timeframe)?	yes		
5. Were the definitions, inclusion and exclusion criteria, algorithms or processes used to identify or select cases and controls valid, reliable, and implemented consistently across all study participants?	yes		
6. Were the cases clearly defined and differentiated from controls?	yes		
7. If less than 100 percent of eligible cases and/or controls were selected for the study, were the cases and/or controls randomly selected from those eligible?			NA
8. Was there use of concurrent controls?	yes		

Criteria	Yes	No	Other (CD, NR, NA)*
9. Were the investigators able to confirm that the exposure/risk occurred prior to the development of the condition or event that defined a participant as a case?	yes		
10. Were the measures of exposure/risk clearly defined, valid, reliable, and implemented consistently (including the same time period) across all study participants?			no
11. Were the assessors of exposure/risk blinded to the case or control status of participants?		no	
12. Were key potential confounding variables measured and adjusted statistically in the analyses? If matching was used, did the investigators account for matching during study analysis?		no	

Quality Rating (Good, Fair, or Poor): **Good**

*CD, cannot determine; NA, not applicable; NR, not reported

7. Study: Das et al. 1983

Criteria	Yes	No	Other (CD, NR, NA)*
1. Was the research question or objective in this paper clearly stated and appropriate?	yes		
2. Was the study population clearly specified and defined?	yes		

Criteria	Yes	No	Other (CD, NR, NA)*
3. Did the authors include a sample size justification?	yes		
4. Were controls selected or recruited from the same or similar population that gave rise to the cases (including the same timeframe)?	yes		
5. Were the definitions, inclusion and exclusion criteria, algorithms or processes used to identify or select cases and controls valid, reliable, and implemented consistently across all study participants?			CD
6. Were the cases clearly defined and differentiated from controls?	yes		
7. If less than 100 percent of eligible cases and/or controls were selected for the study, were the cases and/or controls randomly selected from those eligible?			NA
8. Was there use of concurrent controls?	yes		
9. Were the investigators able to confirm that the exposure/risk occurred prior to the development of the condition or event that defined a participant as a case?	yes		
10. Were the measures of exposure/risk clearly defined, valid, reliable, and implemented consistently (including the same time period) across all study participants?			CD
11. Were the assessors of exposure/risk blinded to the case or control status of participants?		no	

Criteria	Yes	No	Other (CD, NR, NA)*
12. Were key potential confounding variables measured and adjusted statistically in the analyses? If matching was used, did the investigators account for matching during study analysis?		no	

Quality Rating (Good, Fair, or Poor): **Fair**
Comment: Data obtained from abstract only, unable to obtain full PDF of study

*CD, cannot determine; NA, not applicable; NR, not reported

8. Study: Dias 1985

Criteria	Yes	No	Other (CD, NR, NA)*
1. Was the research question or objective in this paper clearly stated and appropriate?	yes		
2. Was the study population clearly specified and defined?	yes		
3. Did the authors include a sample size justification?	yes		
4. Were controls selected or recruited from the same or similar population that gave rise to the cases (including the same timeframe)?		no	
5. Were the definitions, inclusion and exclusion criteria, algorithms or processes used to identify or select cases and controls valid, reliable, and implemented consistently across all study participants?	yes		
6. Were the cases clearly defined and differentiated from controls?		No	

Criteria	Yes	No	Other (CD, NR, NA)*
7. If less than 100 percent of eligible cases and/or controls were selected for the study, were the cases and/or controls randomly selected from those eligible?			NA
8. Was there use of concurrent controls?		no	
9. Were the investigators able to confirm that the exposure/risk occurred prior to the development of the condition or event that defined a participant as a case?	yes		
10. Were the measures of exposure/risk clearly defined, valid, reliable, and implemented consistently (including the same time period) across all study participants?			NA
11. Were the assessors of exposure/risk blinded to the case or control status of participants?		no	
12. Were key potential confounding variables measured and adjusted statistically in the analyses? If matching was used, did the investigators account for matching during study analysis?		no	

Quality Rating (Good, Fair, or Poor): **Fair**
Comment: no control group used

*CD, cannot determine; NA, not applicable; NR, not reported

9. Study: Dayal et al. 1985

Criteria	Yes	No	Other (CD, NR, NA)*

Criteria	Yes	No	Other (CD, NR, NA)*
1. Was the research question or objective in this paper clearly stated and appropriate?	yes		
2. Was the study population clearly specified and defined?	yes		
3. Did the authors include a sample size justification?	yes		
4. Were controls selected or recruited from the same or similar population that gave rise to the cases (including the same timeframe)?		no	
5. Were the definitions, inclusion and exclusion criteria, algorithms or processes used to identify or select cases and controls valid, reliable, and implemented consistently across all study participants?	yes		
6. Were the cases clearly defined and differentiated from controls?		no	
7. If less than 100 percent of eligible cases and/or controls were selected for the study, were the cases and/or controls randomly selected from those eligible?			NA
8. Was there use of concurrent controls?		no	
9. Were the investigators able to confirm that the exposure/risk occurred prior to the development of the condition or event that defined a participant as a case?	yes		

Criteria	Yes	No	Other (CD, NR, NA)*
10. Were the measures of exposure/risk clearly defined, valid, reliable, and implemented consistently (including the same time period) across all study participants?			NA
11. Were the assessors of exposure/risk blinded to the case or control status of participants?		no	
12. Were key potential confounding variables measured and adjusted statistically in the analyses? If matching was used, did the investigators account for matching during study analysis?		no	

Quality Rating (Good, Fair, or Poor): **Good**

Comment: study did not compare LDH value to controls, but rather compared LDH values across disease stage and severity to explore possible correlation

*CD, cannot determine; NA, not applicable; NR, not reported

10. Study: Singh et al. 1991

Criteria	Yes	No	Other (CD, NR, NA)*
1. Was the research question or objective in this paper clearly stated and appropriate?	yes		
2. Was the study population clearly specified and defined?	yes		
3. Did the authors include a sample size justification?	yes		

Criteria	Yes	No	Other (CD, NR, NA)*
4. Were controls selected or recruited from the same or similar population that gave rise to the cases (including the same timeframe)?	yes		
5. Were the definitions, inclusion and exclusion criteria, algorithms or processes used to identify or select cases and controls valid, reliable, and implemented consistently across all study participants?	yes		
6. Were the cases clearly defined and differentiated from controls?	yes		
7. If less than 100 percent of eligible cases and/or controls were selected for the study, were the cases and/or controls randomly selected from those eligible?			NA
8. Was there use of concurrent controls?	yes		
9. Were the investigators able to confirm that the exposure/risk occurred prior to the development of the condition or event that defined a participant as a case?	yes		
10. Were the measures of exposure/risk clearly defined, valid, reliable, and implemented consistently (including the same time period) across all study participants?			NA
11. Were the assessors of exposure/risk blinded to the case or control status of participants?		No	
12. Were key potential confounding variables measured and adjusted statistically in the analyses? If matching was used, did the investigators		No	

Criteria	Yes	No	Other (CD, NR, NA)*
account for matching during study analysis?			

Quality Rating (Good, Fair, or Poor): **Good**

*CD, cannot determine; NA, not applicable; NR, not reported

11. Study: Mukhopadhyay et al. 2008

Criteria	Yes	No	Other (CD, NR, NA)*
1. Was the research question or objective in this paper clearly stated and appropriate?	yes		
2. Was the study population clearly specified and defined?	yes		
3. Did the authors include a sample size justification?	yes		
4. Were controls selected or recruited from the same or similar population that gave rise to the cases (including the same timeframe)?	yes		
5. Were the definitions, inclusion and exclusion criteria, algorithms or processes used to identify or select cases and controls valid, reliable, and implemented consistently across all study participants?	yes		
6. Were the cases clearly defined and differentiated from controls?	yes		

Criteria	Yes	No	Other (CD, NR, NA)*
7. If less than 100 percent of eligible cases and/or controls were selected for the study, were the cases and/or controls randomly selected from those eligible?			NA
8. Was there use of concurrent controls?	yes		
9. Were the investigators able to confirm that the exposure/risk occurred prior to the development of the condition or event that defined a participant as a case?	yes		
10. Were the measures of exposure/risk clearly defined, valid, reliable, and implemented consistently (including the same time period) across all study participants?			NA
11. Were the assessors of exposure/risk blinded to the case or control status of participants?		no	
12. Were key potential confounding variables measured and adjusted statistically in the analyses? If matching was used, did the investigators account for matching during study analysis?		no	

Quality Rating (Good, Fair, or Poor): **Good**
*CD, cannot determine; NA, not applicable; NR, not reported

12. Study: Shehata et al. 2016

Criteria	Yes	No	Other (CD, NR, NA)*

Criteria	Yes	No	Other (CD, NR, NA)*
1. Was the research question or objective in this paper clearly stated and appropriate?	yes		
2. Was the study population clearly specified and defined?	yes		
3. Did the authors include a sample size justification?	yes		
4. Were controls selected or recruited from the same or similar population that gave rise to the cases (including the same timeframe)?	yes		
5. Were the definitions, inclusion and exclusion criteria, algorithms or processes used to identify or select cases and controls valid, reliable, and implemented consistently across all study participants?	yes		
6. Were the cases clearly defined and differentiated from controls?	yes		
7. If less than 100 percent of eligible cases and/or controls were selected for the study, were the cases and/or controls randomly selected from those eligible?			NA
8. Was there use of concurrent controls?	yes		
9. Were the investigators able to confirm that the exposure/risk occurred prior to the development of the condition or event that defined a participant as a case?	yes		

Criteria	Yes	No	Other (CD, NR, NA)*
10. Were the measures of exposure/risk clearly defined, valid, reliable, and implemented consistently (including the same time period) across all study participants?			NA
11. Were the assessors of exposure/risk blinded to the case or control status of participants?		no	
12. Were key potential confounding variables measured and adjusted statistically in the analyses? If matching was used, did the investigators account for matching during study analysis?		no	

Quality Rating (Good, Fair, or Poor): **Good**
*CD, cannot determine; NA, not applicable; NR, not reported

13. Study: Abramson et al. 1989

Criteria	Yes	No	Other (CD, NR, NA)*
1. Was the research question or objective in this paper clearly stated and appropriate?	yes		
2. Was the study population clearly specified and defined?	yes		
3. Did the authors include a sample size justification?	yes		

Criteria	Yes	No	Other (CD, NR, NA)*
4. Were controls selected or recruited from the same or similar population that gave rise to the cases (including the same timeframe)?		no	
5. Were the definitions, inclusion and exclusion criteria, algorithms or processes used to identify or select cases and controls valid, reliable, and implemented consistently across all study participants?	yes		
6. Were the cases clearly defined and differentiated from controls?		no	
7. If less than 100 percent of eligible cases and/or controls were selected for the study, were the cases and/or controls randomly selected from those eligible?			NA
8. Was there use of concurrent controls?		no	
9. Were the investigators able to confirm that the exposure/risk occurred prior to the development of the condition or event that defined a participant as a case?	yes		
10. Were the measures of exposure/risk clearly defined, valid, reliable, and implemented consistently (including the same time period) across all study participants?			NA
11. Were the assessors of exposure/risk blinded to the case or control status of participants?		no	
12. Were key potential confounding variables measured and adjusted statistically in the analyses? If matching was used, did the investigators		no	

Criteria	Yes	No	Other (CD, NR, NA)*
account for matching during study analysis?			

Quality Rating (Good, Fair, or Poor): **Fair**
Comments: no controls were used in this study
*CD, cannot determine; NA, not applicable; NR, not reported

14. Study: Comoy et al. 1990

Criteria	Yes	No	Other (CD, NR, NA)*
1. Was the research question or objective in this paper clearly stated and appropriate?	yes		
2. Was the study population clearly specified and defined?	yes		
3. Did the authors include a sample size justification?			CD
4. Were controls selected or recruited from the same or similar population that gave rise to the cases (including the same timeframe)?	yes		
5. Were the definitions, inclusion and exclusion criteria, algorithms or processes used to identify or select cases and controls valid, reliable, and implemented consistently across all study participants?			CD
6. Were the cases clearly defined and differentiated from controls?	Yes		

Criteria	Yes	No	Other (CD, NR, NA)*
7. If less than 100 percent of eligible cases and/or controls were selected for the study, were the cases and/or controls randomly selected from those eligible?			NA
8. Was there use of concurrent controls?	yes		
9. Were the investigators able to confirm that the exposure/risk occurred prior to the development of the condition or event that defined a participant as a case?			CD
10. Were the measures of exposure/risk clearly defined, valid, reliable, and implemented consistently (including the same time period) across all study participants?			CD
11. Were the assessors of exposure/risk blinded to the case or control status of participants?			CD
12. Were key potential confounding variables measured and adjusted statistically in the analyses? If matching was used, did the investigators account for matching during study analysis?			CD

Quality Rating (Good, Fair, or Poor): **Fair**
Comment: unable to obtain full PDF of study, only abstract was assessed.
*CD, cannot determine; NA, not applicable; NR, not reported

15. Study: Nakajima et al. 1986

Criteria	Yes	No	Other (CD, NR, NA)*

Criteria	Yes	No	Other (CD, NR, NA)*
1. Was the research question or objective in this paper clearly stated and appropriate?	yes		
2. Was the study population clearly specified and defined?	yes		
3. Did the authors include a sample size justification?	yes		
4. Were controls selected or recruited from the same or similar population that gave rise to the cases (including the same timeframe)?		no	
5. Were the definitions, inclusion and exclusion criteria, algorithms or processes used to identify or select cases and controls valid, reliable, and implemented consistently across all study participants?	yes		
6. Were the cases clearly defined and differentiated from controls?			NA
7. If less than 100 percent of eligible cases and/or controls were selected for the study, were the cases and/or controls randomly selected from those eligible?			NA
8. Was there use of concurrent controls?		No	
9. Were the investigators able to confirm that the exposure/risk occurred prior to the development of the condition or event that defined a participant as a case?	yes		

Criteria	Yes	No	Other (CD, NR, NA)*
10. Were the measures of exposure/risk clearly defined, valid, reliable, and implemented consistently (including the same time period) across all study participants?			NA
11. Were the assessors of exposure/risk blinded to the case or control status of participants?		No	
12. Were key potential confounding variables measured and adjusted statistically in the analyses? If matching was used, did the investigators account for matching during study analysis?		No	

Quality Rating (Good, Fair, or Poor): **Good**

Comment: not a case-control study. Reliable Investigation of isoenzyme pattern seen in Rb patients
*CD, cannot determine; NA, not applicable; NR, not reported

16. Study: Shine et al. 1990

Criteria	Yes	No	Other (CD, NR, NA)*
1. Was the research question or objective in this paper clearly stated and appropriate?	yes		
2. Was the study population clearly specified and defined?	yes		
3. Did the authors include a sample size justification?	yes		
4. Were controls selected or recruited from the same or similar		no	

Criteria	Yes	No	Other (CD, NR, NA)*
population that gave rise to the cases (including the same timeframe)?			
5. Were the definitions, inclusion and exclusion criteria, algorithms or processes used to identify or select cases and controls valid, reliable, and implemented consistently across all study participants?	yes		
6. Were the cases clearly defined and differentiated from controls?			NA
7. If less than 100 percent of eligible cases and/or controls were selected for the study, were the cases and/or controls randomly selected from those eligible?			NA
8. Was there use of concurrent controls?		No	
9. Were the investigators able to confirm that the exposure/risk occurred prior to the development of the condition or event that defined a participant as a case?	yes		
10. Were the measures of exposure/risk clearly defined, valid, reliable, and implemented consistently (including the same time period) across all study participants?			NA
11. Were the assessors of exposure/risk blinded to the case or control status of participants?		No	
12. Were key potential confounding variables measured and adjusted statistically in the analyses? If matching was used, did the investigators account for matching during study analysis?		No	

17. Study: Wu et al. 1997

Criteria	Yes	No	Other (CD, NR, NA)*
1. Was the research question or objective in this paper clearly stated and appropriate?	yes		
2. Was the study population clearly specified and defined?	yes		
3. Did the authors include a sample size justification?	yes		
4. Were controls selected or recruited from the same or similar population that gave rise to the cases (including the same timeframe)?		no	
5. Were the definitions, inclusion and exclusion criteria, algorithms or processes used to identify or select cases and controls valid, reliable, and implemented consistently across all study participants?	yes		
6. Were the cases clearly defined and differentiated from controls?			NA
7. If less than 100 percent of eligible cases and/or controls were selected for the study, were the cases and/or controls randomly selected from those eligible?			NA
8. Was there use of concurrent controls?		No	

Criteria	Yes	No	Other (CD, NR, NA)*
9. Were the investigators able to confirm that the exposure/risk occurred prior to the development of the condition or event that defined a participant as a case?	yes		
10. Were the measures of exposure/risk clearly defined, valid, reliable, and implemented consistently (including the same time period) across all study participants?			NA
11. Were the assessors of exposure/risk blinded to the case or control status of participants?		No	
12. Were key potential confounding variables measured and adjusted statistically in the analyses? If matching was used, did the investigators account for matching during study analysis?		No	

Quality Rating (Good, Fair, or Poor): **Good**
Comment: not a case-control study. Reliable Investigation of isoenzyme pattern seen in Rb patients
*CD, cannot determine; NA, not applicable; NR, not reported

18. Study: Shehata et al. 2010

Criteria	Yes	No	Other (CD, NR, NA)*
1. Was the research question or objective in this paper clearly stated and appropriate?	yes		
2. Was the study population clearly specified and defined?	yes		

Criteria	Yes	No	Other (CD, NR, NA)*
3. Did the authors include a sample size justification?	yes		
4. Were controls selected or recruited from the same or similar population that gave rise to the cases (including the same timeframe)?	yes		
5. Were the definitions, inclusion and exclusion criteria, algorithms or processes used to identify or select cases and controls valid, reliable, and implemented consistently across all study participants?	yes		
6. Were the cases clearly defined and differentiated from controls?	yes		
7. If less than 100 percent of eligible cases and/or controls were selected for the study, were the cases and/or controls randomly selected from those eligible?			NA
8. Was there use of concurrent controls?	yes		
9. Were the investigators able to confirm that the exposure/risk occurred prior to the development of the condition or event that defined a participant as a case?	yes		
10. Were the measures of exposure/risk clearly defined, valid, reliable, and implemented consistently (including the same time period) across all study participants?			NA
11. Were the assessors of exposure/risk blinded to the case or control status of participants?		no	

Criteria	Yes	No	Other (CD, NR, NA)*
12. Were key potential confounding variables measured and adjusted statistically in the analyses? If matching was used, did the investigators account for matching during study analysis?		no	

Quality Rating (Good, Fair, or Poor): **Good**
*CD, cannot determine; NA, not applicable; NR, not reported

19. Study: Mendelsohn et al. 1998

Criteria	Yes	No	Other (CD, NR, NA)*
1. Was the research question or objective in this paper clearly stated and appropriate?	yes		
2. Was the study population clearly specified and defined?	yes		
3. Did the authors include a sample size justification?	yes		
4. Were controls selected or recruited from the same or similar population that gave rise to the cases (including the same timeframe)?	yes		
5. Were the definitions, inclusion and exclusion criteria, algorithms or processes used to identify or select cases and controls valid, reliable, and implemented consistently across all study participants?	yes		
6. Were the cases clearly defined and differentiated from controls?	yes		

Criteria	Yes	No	Other (CD, NR, NA)*
7. If less than 100 percent of eligible cases and/or controls were selected for the study, were the cases and/or controls randomly selected from those eligible?			NA
8. Was there use of concurrent controls?	yes		
9. Were the investigators able to confirm that the exposure/risk occurred prior to the development of the condition or event that defined a participant as a case?	yes		
10. Were the measures of exposure/risk clearly defined, valid, reliable, and implemented consistently (including the same time period) across all study participants?			NA
11. Were the assessors of exposure/risk blinded to the case or control status of participants?		no	
12. Were key potential confounding variables measured and adjusted statistically in the analyses? If matching was used, did the investigators account for matching during study analysis?		no	

Quality Rating (Good, Fair, or Poor): **Good**
*CD, cannot determine; NA, not applicable; NR, not reported

20. Study: Dias 1979

Criteria	Yes	No	Other (CD, NR, NA)*

Criteria	Yes	No	Other (CD, NR, NA)*
1. Was the research question or objective in this paper clearly stated and appropriate?	yes		
2. Was the study population clearly specified and defined?	yes		
3. Did the authors include a sample size justification?	yes		
4. Were controls selected or recruited from the same or similar population that gave rise to the cases (including the same timeframe)?	yes		
5. Were the definitions, inclusion and exclusion criteria, algorithms or processes used to identify or select cases and controls valid, reliable, and implemented consistently across all study participants?	yes		
6. Were the cases clearly defined and differentiated from controls?	yes		
7. If less than 100 percent of eligible cases and/or controls were selected for the study, were the cases and/or controls randomly selected from those eligible?			NA
8. Was there use of concurrent controls?	yes		
9. Were the investigators able to confirm that the exposure/risk occurred prior to the development of the condition or event that defined a participant as a case?	yes		

Criteria	Yes	No	Other (CD, NR, NA)*
10. Were the measures of exposure/risk clearly defined, valid, reliable, and implemented consistently (including the same time period) across all study participants?			NA
11. Were the assessors of exposure/risk blinded to the case or control status of participants?		no	
12. Were key potential confounding variables measured and adjusted statistically in the analyses? If matching was used, did the investigators account for matching during study analysis?		no	

Quality Rating (Good, Fair, or Poor): **Good**
Comment: no p-value determined
*CD, cannot determine; NA, not applicable; NR, not reported

21. Study: Hadjistilianou et al. 2012

Criteria	Yes	No	Other (CD, NR, NA)*
1. Was the research question or objective in this paper clearly stated and appropriate?	yes		
2. Was the study population clearly specified and defined?	yes		
3. Did the authors include a sample size justification?	yes		
4. Were controls selected or recruited from the same or similar population that gave rise to the cases (including the same timeframe)?	yes		

Criteria	Yes	No	Other (CD, NR, NA)*
5. Were the definitions, inclusion and exclusion criteria, algorithms or processes used to identify or select cases and controls valid, reliable, and implemented consistently across all study participants?	yes		
6. Were the cases clearly defined and differentiated from controls?	yes		
7. If less than 100 percent of eligible cases and/or controls were selected for the study, were the cases and/or controls randomly selected from those eligible?			NA
8. Was there use of concurrent controls?	yes		
9. Were the investigators able to confirm that the exposure/risk occurred prior to the development of the condition or event that defined a participant as a case?	yes		
10. Were the measures of exposure/risk clearly defined, valid, reliable, and implemented consistently (including the same time period) across all study participants?			NA
11. Were the assessors of exposure/risk blinded to the case or control status of participants?		no	
12. Were key potential confounding variables measured and adjusted statistically in the analyses? If matching was used, did the investigators account for matching during study analysis?		no	

Quality Rating (Good, Fair, or Poor): **Good**

22. Study: Cheng et al. 2017

Criteria	Yes	No	Other (CD, NR, NA)*
1. Was the research question or objective in this paper clearly stated and appropriate?	yes		
2. Was the study population clearly specified and defined?	yes		
3. Did the authors include a sample size justification?	yes		
4. Were controls selected or recruited from the same or similar population that gave rise to the cases (including the same timeframe)?		no	
5. Were the definitions, inclusion and exclusion criteria, algorithms or processes used to identify or select cases and controls valid, reliable, and implemented consistently across all study participants?	yes		
6. Were the cases clearly defined and differentiated from controls?		no	
7. If less than 100 percent of eligible cases and/or controls were selected for the study, were the cases and/or controls randomly selected from those eligible?			NA
8. Was there use of concurrent controls?		no	
9. Were the investigators able to confirm that the exposure/risk occurred prior to the development of the condition or event that defined a participant as a case?	yes		

Criteria	Yes	No	Other (CD, NR, NA)*
10. Were the measures of exposure/risk clearly defined, valid, reliable, and implemented consistently (including the same time period) across all study participants?			NA
11. Were the assessors of exposure/risk blinded to the case or control status of participants?		no	
12. Were key potential confounding variables measured and adjusted statistically in the analyses? If matching was used, did the investigators account for matching during study analysis?		no	

Quality Rating (Good, Fair, or Poor): **Good**

Comment: No controls used in study, mostly laboratory analysis of the proteins found in AH

23. Study: Cheng et al. 2017'

Criteria	Yes	No	Other (CD, NR, NA)*
1. Was the research question or objective in this paper clearly stated and appropriate?	yes		
2. Was the study population clearly specified and defined?	yes		
3. Did the authors include a sample size justification?			CD
4. Were controls selected or recruited from the same or similar	yes		

Criteria	Yes	No	Other (CD, NR, NA)*
population that gave rise to the cases (including the same timeframe)?			
5. Were the definitions, inclusion and exclusion criteria, algorithms or processes used to identify or select cases and controls valid, reliable, and implemented consistently across all study participants?			CD
6. Were the cases clearly defined and differentiated from controls?	Yes		
7. If less than 100 percent of eligible cases and/or controls were selected for the study, were the cases and/or controls randomly selected from those eligible?			NA
8. Was there use of concurrent controls?	yes		
9. Were the investigators able to confirm that the exposure/risk occurred prior to the development of the condition or event that defined a participant as a case?			CD
10. Were the measures of exposure/risk clearly defined, valid, reliable, and implemented consistently (including the same time period) across all study participants?			CD
11. Were the assessors of exposure/risk blinded to the case or control status of participants?			CD
12. Were key potential confounding variables measured and adjusted statistically in the analyses? If matching was used, did the investigators account for matching during study analysis?			CD

Quality Rating (Good, Fair, or Poor): **Fair**
Comment: unable to obtain full PDF of study, only abstract was assessed.

24. Study: Abramson et al. 1978

Criteria	Yes	No	Other (CD, NR, NA)*
1. Was the research question or objective in this paper clearly stated and appropriate?	yes		
2. Was the study population clearly specified and defined?	yes		
3. Did the authors include a sample size justification?			CD
4. Were controls selected or recruited from the same or similar population that gave rise to the cases (including the same timeframe)?			CD
5. Were the definitions, inclusion and exclusion criteria, algorithms or processes used to identify or select cases and controls valid, reliable, and implemented consistently across all study participants?			CD
6. Were the cases clearly defined and differentiated from controls?			CD
7. If less than 100 percent of eligible cases and/or controls were selected for the study, were the cases and/or controls randomly selected from those eligible?		NA	
8. Was there use of concurrent controls?			CD
9. Were the investigators able to confirm that the exposure/risk occurred prior to the development of the condition or event that defined a			CD

Criteria	Yes	No	Other (CD, NR, NA)*
participant as a case?			
10. Were the measures of exposure/risk clearly defined, valid, reliable, and implemented consistently (including the same time period) across all study participants?			CD
11. Were the assessors of exposure/risk blinded to the case or control status of participants?			CD
12. Were key potential confounding variables measured and adjusted statistically in the analyses? If matching was used, did the investigators account for matching during study analysis?			CD

Quality Rating (Good, Fair, or Poor): **Fair**
Comment: unable to obtain full PDF of study, only abstract was assessed.

25. Study: Abramson et al. 1993

Criteria	Yes	No	Other (CD, NR, NA)*
1. Was the research question or objective in this paper clearly stated and appropriate?	yes		
2. Was the study population clearly specified and defined?	yes		
3. Did the authors include a sample size justification?			CD

Criteria	Yes	No	Other (CD, NR, NA)*
4. Were controls selected or recruited from the same or similar population that gave rise to the cases (including the same timeframe)?			CD
5. Were the definitions, inclusion and exclusion criteria, algorithms or processes used to identify or select cases and controls valid, reliable, and implemented consistently across all study participants?			CD
6. Were the cases clearly defined and differentiated from controls?	Yes		
7. If less than 100 percent of eligible cases and/or controls were selected for the study, were the cases and/or controls randomly selected from those eligible?			NA
8. Was there use of concurrent controls?			CD
9. Were the investigators able to confirm that the exposure/risk occurred prior to the development of the condition or event that defined a participant as a case?			CD
10. Were the measures of exposure/risk clearly defined, valid, reliable, and implemented consistently (including the same time period) across all study participants?			CD
11. Were the assessors of exposure/risk blinded to the case or control status of participants?			CD
12. Were key potential confounding variables measured and adjusted statistically in the analyses? If matching was used, did the investigators			CD

Criteria	Yes	No	Other (CD, NR, NA)*
account for matching during study analysis?			

Quality Rating (Good, Fair, or Poor): **Fair**
Comment: Unable to obtain full PDF of study, only abstract was assessed.

26. Study: Berry et al. 2017

Criteria	Yes	No	Other (CD, NR, NA)*
1. Was the research question or objective in this paper clearly stated and appropriate?	yes		
2. Was the study population clearly specified and defined?	yes		
3. Did the authors include a sample size justification?	yes		
4. Were controls selected or recruited from the same or similar population that gave rise to the cases (including the same timeframe)?	yes		
5. Were the definitions, inclusion and exclusion criteria, algorithms or processes used to identify or select cases and controls valid, reliable, and implemented consistently across all study participants?	yes		
6. Were the cases clearly defined and differentiated from controls?	yes		

Criteria	Yes	No	Other (CD, NR, NA)*
7. If less than 100 percent of eligible cases and/or controls were selected for the study, were the cases and/or controls randomly selected from those eligible?			NA
8. Was there use of concurrent controls?	yes		
9. Were the investigators able to confirm that the exposure/risk occurred prior to the development of the condition or event that defined a participant as a case?	yes		
10. Were the measures of exposure/risk clearly defined, valid, reliable, and implemented consistently (including the same time period) across all study participants?			NA
11. Were the assessors of exposure/risk blinded to the case or control status of participants?		no	
12. Were key potential confounding variables measured and adjusted statistically in the analyses? If matching was used, did the investigators account for matching during study analysis?		no	

Quality Rating (Good, Fair, or Poor): **Good**
*CD, cannot determine; NA, not applicable; NR, not reported

27. Study: Berry et al. 2018

Criteria	Yes	No	Other (CD, NR, NA)*

Criteria	Yes	No	Other (CD, NR, NA)*
1. Was the research question or objective in this paper clearly stated and appropriate?	yes		
2. Was the study population clearly specified and defined?	yes		
3. Did the authors include a sample size justification?	yes		
4. Were controls selected or recruited from the same or similar population that gave rise to the cases (including the same timeframe)?	yes		
5. Were the definitions, inclusion and exclusion criteria, algorithms or processes used to identify or select cases and controls valid, reliable, and implemented consistently across all study participants?	yes		
6. Were the cases clearly defined and differentiated from controls?	yes		
7. If less than 100 percent of eligible cases and/or controls were selected for the study, were the cases and/or controls randomly selected from those eligible?			NA
8. Was there use of concurrent controls?	yes		
9. Were the investigators able to confirm that the exposure/risk occurred prior to the development of the condition or event that defined a participant as a case?	yes		

Criteria	Yes	No	Other (CD, NR, NA)*
10. Were the measures of exposure/risk clearly defined, valid, reliable, and implemented consistently (including the same time period) across all study participants?			NA
11. Were the assessors of exposure/risk blinded to the case or control status of participants?		no	
12. Were key potential confounding variables measured and adjusted statistically in the analyses? If matching was used, did the investigators account for matching during study analysis?		no	

Quality Rating (Good, Fair, or Poor): **Good**
*CD, cannot determine; NA, not applicable; NR, not reported