## APPENDIX 1 - Complete search strategy on databases

#### PubMed

- #1 Search ((((((((((""Outcome Assessment (Health Care)""[Mesh]) OR ""Patient Outcome Assessment""[Mesh]) AND ""Drug Therapy""[Mesh]) OR ""Polypharmacy""[Mesh]) OR Complexity) OR ""Drug therapy complexity"") OR ""Medication complexity"") OR ""Medication regimen complexity"") OR ""Regimen complexity"") OR ""Treatment complexity"") AND ""Medication regimen complexity index"") OR ""MRCI""

## Scopus

- #1 (ALL ("Medication regimen complexity index") OR ALL ("MRCI"))
- #2 (ALL ("Drug Therapy") OR ALL ("Therapy, Drug") OR ALL ("Drug Therapies") OR ALL (
  "Therapies, Drug") OR ALL (chemotherapy) OR ALL (chemotherapies) OR ALL (
  pharmacotherapy) OR ALL (pharmacotherapies) OR ALL (polypharmacy) OR ALL (
  complexity) OR ALL ("Drug therapy complexity") OR ALL ("Medication complexity") OR ALL ("Regimen complexity") OR ALL ("Treatment complexity"))
- #3 (ALL ("Outcome assessment") OR ALL ("Assessment, Outcome") OR ALL ("Assessments, Outcome") OR ALL ("Outcome Assessments") OR ALL ("Outcomes Assessment") OR ALL ("Assessment, Outcomes") OR ALL ("Outcomes Assessments") OR ALL ("Outcomes Research") OR ALL ("Research, Outcomes") OR ALL ("Outcome Studies") OR ALL ("Outcome Study") OR ALL ("Studies, Outcome") OR ALL ("Study, Outcome") OR ALL ("Outcome Measures") OR ALL ("Measure, Outcome") OR ALL ("Measures, Outcome") OR ALL ("Outcome Measure") OR ALL ("Patient Outcome Assessment") OR ALL ("Patient Outcome Assessments, Patient") OR ALL ("Patient Outcomes") OR ALL ("Assessments, Patient") OR ALL ("Patient Outcomes") OR ALL ("Patient Outcomes") OR ALL ("Patient Outcomes Research") OR ALL ("Patient Centered Outcomes Research") OR ALL ("Patient Centered Outcomes Research") OR ALL ("Research, Patient Outcomes") OR ALL ("Research, Patient Outcomes") OR ALL ("Outcome Assessment, Patient")
- **#4** #1 AND #2 AND #3
- #5 ((ALL ("Medication regimen complexity index") OR ALL ("MRCI"))) AND ((ALL ("Drug Therapy") OR ALL ("Therapy, Drug") OR ALL ("Drug Therapies") OR ALL ("Therapies, Drug") OR ALL (chemotherapy) OR ALL (chemotherapy) OR ALL (chemotherapy) OR ALL (pharmacotherapy) OR ALL (pharmacotherapy) OR ALL (pharmacotherapy) OR ALL ("Drug therapy complexity") OR ALL ("Medication complexity") OR ALL ("Medication regimen") OR ALL ("Medication regimen complexity") OR ALL ("Regimen complexity") OR ALL ("Treatment complexity")) AND ((ALL ("Outcome assessment") OR ALL ("Assessment, Outcome") OR ALL ("Assessments, Outcome") OR ALL ("Outcome Assessments") OR ALL ("Outcomes Assessments") OR ALL ("Research, Outcomes") OR ALL ("Outcomes Research") OR ALL ("Research, Outcomes") OR ALL ("Outcome Studies") OR ALL ("Outcome Study") OR ALL ("Research, Outcomes") OR ALL ("Outcome Study") OR ALL ("Research, Outcomes") OR ALL ("Outcome Study") OR ALL ("Outcome S

("Studies, Outcome") OR ALL ("Study, Outcome") OR ALL ("Outcome Measures") OR ALL ("Measure, Outcome") OR ALL ("Outcome Measure") OR ALL ("Patient Outcome Assessment") OR ALL ("Assessments, Patient Outcome") OR ALL ("Outcome Assessments, Patient") OR ALL ("Patient Outcome Assessments") OR ALL ("Assessment, Patient Outcomes") OR ALL ("Patient Outcomes Assessment") OR ALL ("Outcomes Assessments, Patient") OR ALL ("Patient-Centered Outcomes Research") OR ALL ("Patient Centered Outcomes Research") OR ALL ("Research, Patient-Centered Outcomes") OR ALL ("Assessment, Patient Outcome") OR ALL ("Outcome Assessment, Patient")))

#### Embase

- "outcome assessment' OR 'assessment, outcome' OR 'assessments, outcome' OR 'outcome assessments' OR 'outcomes assessment' OR' assessment, outcomes' OR 'assessments, outcomes' OR 'outcomes assessments' OR 'outcomes research' OR 'research, outcomes' OR 'outcome studies' OR 'outcome study' OR 'studies, outcome' OR 'study, outcome' OR 'outcome measures' OR 'measure, outcome' OR 'measures, outcome' OR 'outcome measure' OR 'patient outcome assessment' OR 'assessments, patient outcome of OR 'outcome assessments, patient outcomes' OR 'patient outcomes assessment' OR 'outcomes assessment, patient outcomes' OR 'patient outcomes research' OR 'patient centered outcomes research' OR 'research, patient-centered outcomes' OR 'assessment, patient outcome' OR' outcome assessment, patient'
- 'drug therapy' OR 'therapy, drug' OR 'drug therapies' OR 'therapies, drug' OR 'chemotherapy' OR 'chemotherapies' OR 'pharmacotherapy' OR' pharmacotherapies' OR 'complexity' OR 'medication complexity' OR 'drug therapy complexity' OR 'regimen complexity' OR 'treatment complexity' OR 'medication regimen' OR 'medication regimen complexity' OR 'polypharmacy'
- #3 'medication regimen complexity index' OR 'mrci'
- **#4** #1 AND # 2 AND #3

#### Lilacs

(tw: (((mh:"Outcome assessment") OR "Assessment, Outcome" OR "Assessments, Outcome" OR "Outcome Assessments" OR "Outcomes Assessment" OR "Assessment, Outcomes" OR "Assessments, Outcomes" OR "Outcomes Assessments" OR "Outcomes Research" OR "Research, Outcomes" OR "Outcome Studies" OR "Outcome Study" OR "Studies, Outcome" OR "Study, Outcome" OR "Outcome Measures" OR "Measure, Outcome" OR "Measures, Outcome" OR "Outcome Measure" OR (mh:"Patient Outcome Assessment") OR "Assessments, Patient Outcome" OR "Outcome Assessments, Patient Outcomes Assessment, Patient Outcomes Assessment" OR "Outcomes Assessment, Patient Outcomes Assessment" OR "Patient Centered Outcomes Research" OR "Patient Centered Outcomes Research" OR "Research, Patient-Centered Outcomes" OR "Assessment, Patient Outcome" OR "Outcome Assessment, Patient"))) AND (tw:( ((mh:"Drug Therapy") OR "Therapy, Drug" OR "Drug Therapies" OR "Therapies, Drug" OR "Chemotherapy" OR "Chemotherapies" OR "Pharmacotherapy" OR "Pharmacotherapies" OR "Complexity" OR "Medication complexity" OR "Drug therapy complexity" OR "Regimen complexity" OR "Treatment complexity" OR "Medication regimen" OR "Medication regimen complexity" OR (mh:"Polypharmacy")))) AND (tw:(("Medication regimen complexity index" OR "MRCI")))

### Open Thesis

"Outcome assessment" OR "Assessment, Outcome" OR "Assessments, Outcome" OR "Outcome Assessments" OR "Outcomes Assessment" OR "Assessment, Outcomes" OR "Assessments, Outcomes" OR "Outcomes Assessments" OR "Outcomes Research" OR "Research, Outcomes" OR "Outcome Studies" OR "Outcome Study" OR "Studies, Outcome" OR "Study, Outcome" OR "Outcome Measures" OR "Measure, Outcome" OR "Measures, Outcome" OR "Outcome Measure" OR "Patient Outcome Assessment" OR "Assessments, Patient Outcome" OR "Outcome Assessments, Patient Outcomes" OR "Patient Outcomes" OR "Patient Outcomes Assessments, Patient" OR "Patient Outcomes OR "Patient Outcomes Assessments, Patient" OR "Patient-Centered Outcomes Research" OR "Patient Centered Outcomes Research" OR "Research, Patient-Centered Outcomes" OR "Assessment, Patient Outcome" OR "Outcome Assessment, Patient" AND "Drug Therapy" OR "Therapy, Drug" OR "Drug Therapies" OR "Therapies, Drug" OR Chemotherapy OR Chemotherapies OR Pharmacotherapy OR Pharmacotherapies OR Polypharmacy OR Complexity OR "Drug therapy complexity" OR "Medication complexity" OR "Medication regimen" OR "Medication regimen complexity" OR "Regimen complexity" OR "Treatment complexity" AND "Medication regimen complexity index" OR "MRCI"

#### Web of Science

#1 Tópico: ("Outcome assessment") OR Tópico: ("Assessment, Outcome") OR Tópico: ("Assessments, Outcome") OR Tópico: ("Outcome Assessments") OR Tópico: ("Outcomes Assessment") OR Tópico: ("Assessment, Outcomes") OR Tópico: ("Assessments, Outcomes") OR Tópico: ("Outcomes Assessments") OR Tópico: ("Outcomes Research") OR Tópico: ("Research, Outcomes") OR Tópico: ("Outcome Studies") OR Tópico: ("Outcome Study") OR Tópico: ("Studies, Outcome") OR Tópico: ("Study, Outcome") OR Tópico: ("Outcome Measures") OR Tópico: ("Measure, Outcome") OR Tópico: ("Measures, Outcome") OR Tópico: ("Outcome Measure")

Índices=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Tempo estipulado=Todos os anos

Tópico: ("Patient Outcome Assessment") OR Tópico: ("Assessments, Patient Outcome") OR Tópico: ("Outcome Assessments, Patient") OR Tópico: ("Patient Outcome Assessments") OR Tópico: ("Assessment, Patient Outcomes") OR Tópico: ("Patient Outcomes Assessment") OR Tópico: ("Outcomes Assessments, Patient") OR Tópico: ("Patient-Centered Outcomes Research") OR Tópico: ("Patient Centered Outcomes Research") OR Tópico: ("Research, Patient-Centered Outcomes") OR Tópico: ("Assessment, Patient Outcome") OR Tópico: ("Outcome Assessment, Patient")

Índices=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Tempo estipulado=Todos os anos

#3 Tópico: ("Drug Therapy") OR Tópico: ("Therapy, Drug") OR Tópico: ("Drug Therapies") OR Tópico: ("Therapies, Drug") OR Tópico: (Chemotherapy) OR Tópico: (Chemotherapies) OR Tópico: (Pharmacotherapy)OR Tópico: (Pharmacotherapies) OR Tópico: (Polypharmacy) OR Tópico: (Complexity) OR Tópico: ("Drug therapy complexity") OR Tópico: ("Medication complexity") OR Tópico: ("Medication regimen") OR Tópico: ("Medication regimen complexity") OR Tópico: ("Regimen complexity") OR Tópico: ("Treatment complexity")

Índices=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Tempo estipulado=Todos os anos

#4 Tópico: ("Medication regimen complexity index") OR Tópico: ("MRCI")

Índices=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Tempo estipulado=Todos os anos

**#5** #2 OR #1

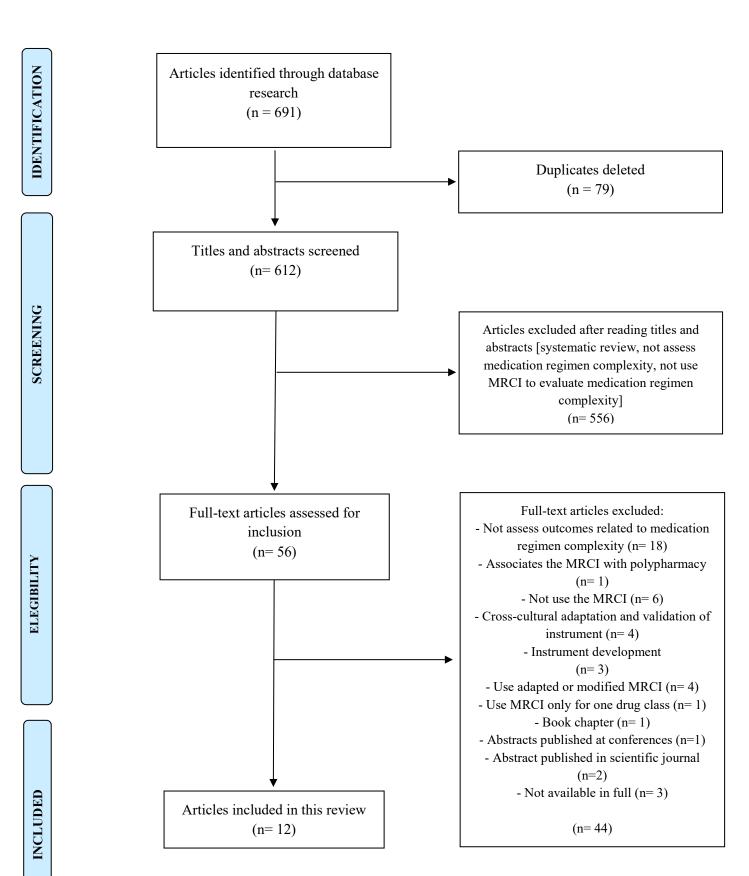
Índices=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Tempo estipulado=Todos os anos

**#6** #5 AND #4 AND #3

Índices=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Tempo estipulado=Todos os anos

#### • The Cochrane Library

- "Outcome assessment" or "Assessment, Outcome" or "Assessments, Outcome" or "Outcome Assessments" or "Outcomes Assessment" or "Assessment, Outcomes" or "Assessments, Outcomes" or "Outcomes Assessments" or "Outcomes Research" or "Research, Outcomes" or "Outcome Studies" or "Outcome Study" or "Studies, Outcome" or "Study, Outcome" or "Outcome Measures" or "Measure, Outcome" or "Measures, Outcome" or "Outcome Measure" or "Patient Outcome Assessment" or "Assessments, Patient Outcome or "Outcome Assessments, Patient" or "Patient Outcomes Assessment" or "Outcomes Assessment" or "Outcomes Research" or "Patient-Centered Outcomes Research" or "Patient Centered Outcomes Research" or "Research, Patient-Centered Outcomes" or "Assessment, Patient Outcomes, Patient" (Word variations have been searched)
- "Drug Therapy" or "Therapy, Drug" or "Drug Therapies" or "Therapies, Drug" or "Chemotherapy" or "Chemotherapies" or "Pharmacotherapy" or "Pharmacotherapies" or "Complexity" or "Medication complexity" or "Drug therapy complexity" or "Regimen complexity" or "Treatment complexity" or "Medication regimen" or "Medication regimen complexity" or "Polypharmacy"
- #3 "Medication regimen complexity index" or "MRCI"
- **#4** #1 and #2 and #3



# **APPENDIX 3 – List of excluded articles after reviewed of full text**

Author	Title	Journal	Reason for exclusion		
Acurcio et al., 2009	Complexity of therapeutic regimens prescribed for elderly retirees, Belo Horizonte/MG, Brazil	Revista da Associação Medica Brasileira	It did not use the MRCI to measure medication regimen complexity		
Al-Jazairi et al., 2017	Impact of a medication reconciliation program on cardiac surgery patients	Asian Cardiovascular & Thoracic Annals	It did not relate medication regimen complexity with health outcomes, but to discrepancies		
Barnason et al., 2010	Pilot testing of a medication self- management transition intervention for heart failure patients	Western Journal of Nursing Research	It did not relate medication regimen complexity with health outcomes		
Bryant et al., 2016	Evaluating Patient-Level Medication Regimen Complexity Over Time in Heart Transplant Recipients	The Annals of Pharmacotherapy	It did not evaluate health outcomes, just quantified medication regimen complexity		
Cadogan et al., 2016	Appropriate Polypharmacy and Medicine Safety: When Many is not Too Many	Drug Safety	It did not use the MRCI to measure medication regimen complexity		
Cardone et al., 2011	Quantifying home medication regimen changes and quality of life in patients receiving nocturnal home hemodialysis	Hemodialysis international. International Symposium on Home Hemodialysis	It did not evaluate health outcomes, just quantified medication regimen complexity		
Cecere et al., 2012	Adherence to long-acting inhaled therapies among patients with chronic obstructive pulmonary disease (COPD)	International Journal of Chronic Obstructive Pulmonary Disease	It did not use the MRCI to measure medication regimen complexity		
Chang et al., 2017	Medication regimen complexity and prevalence of potentially inappropriate medicines in older patients after hospitalisation	International Journal of Clinical Pharmacy	It did not evaluate health outcomes, just quantified medication regimen complexity		
Cobretti et al., 2017	Medication regimen complexity in ambulatory older adults with heart failure	Clinical Interventions in Aging	It used adapted MRCI		
Correr et al., 2011	Effects of a pharmacotherapy follow-up in community pharmacies on type 2 diabetes patients in Brazil	International Journal of Clinical Pharmacy	It did not relate medication regimen complexity with clinical outcomes		

Author	Title	Journal	Reason for exclusion		
Cortes et al., 2017	Influence of hospital admission in the pharmacotherapy complexity of HIV+ patients	Oficial de Expresion Cientifica de La Sociedad Espanola de Farmacia Hospitalaria	The study measured medication regimen complexity through the MRCI tool adapted by University of Colorado in HIV+ patients		
Pablos-Velasco et al., 2014	Current level of glycaemic control and its associated factors in patients with type 2 diabetes across Europe: data from the PANORAMA study	Clinical Endocrinology	It did not evaluate medication regimen complexity		
Fortuna et al., 2015	Medication regimen complexity evaluation in a hypertensive Portuguese population	International Journal of Clinical Pharmacy	The study was a publication at conferences		
George et al., 2004	Development and validation of the medication regimen complexity index	The Annals of Pharmacotherapy	The study developed and validated a MRCI tool		
Hirsch et al., 2014	Validation of a patient-level medication regimen complexity index as a possible tool to identify patients for medication therapy management intervention	Pharmacotherapy	The study validated the MRCI		
Hirsch et al., 2015		Advances in Medicine and Biology	The study was a book chapters		
Ho et al., 2017	Associations among medication regimen complexity, medical specialty, and medication possession ratio in newly diagnosed hypertensive patients: A population-based study	Medicine	The study used MRCI to newly diagnosed hypertensive patients, without relation with health outcomes		
Kai Sun et al., 2017	Are Chinese-American rheumatology patients who use traditional Chinese medicine less adherent to prescribed western medications? Arthritis and Rheumatology, 69	-	The study was a publication at conferences		
Leblebici et al., 2018	Medication adherence and medication regimen complexity of patients with polypharmacy at community pharmacy setting	International Journal of Clinical Pharmacy	Abstract published in scientific journal		
Lepelley et al., 2018	Electronic Medication Regimen Complexity Index at admission and	International Journal for Quality in Health Care	The study used modified MRCI		

Author	Title	Journal	Reason for exclusion		
	complications during hospitalization in medical wards: a tool to improve quality of care?				
Libby et al., 2013	Patient-level medication regimen complexity across populations with chronic disease	Clinical Therapeutics	It did not relate medication regimen complexity with health outcomes. The study quantified MRCI in patient with chronic disease		
Linnebur et al., 2014	Patient-level medication regimen Clinical Therapeutics complexity in older adults with depression		It did not relate medication regiment complexity with health outcomes. The study quantified MRCI in patient with depression		
Logan et al., 2014	Rates and predictors of adherence to psychotropic medications in children with autism spectrum disorders	Journal of Autism and Developmental Disorders	The study used modified MRCI for patients with autism spectrum disorders		
Martin et al., 2007	The Antiretroviral Regimen Complexity Index. A novel method of quantifying regimen complexity	Journal of Acquired Immune Deficiency Syndromes	The study used modified MRCI. Proposed a method to evaluate the antiretrovirals regimen		
Matza et al., 2014	Health state utilities associated with attributes of treatments for hepatitis C. European Journal of Health Economics	European Journal of Health Economics	It did not use the MRCI to measure medication regimen complexity		
Mcdonald et al., 2013	Automating the medication regimen complexity index. Journal of the American Medical Informatics Association	Journal of the American Medical Informatics Association	The study did not evaluate health outcomes		
Mcdonald et al., 2015	Outcomes of clinical decision support (CDS) and correlates of CDS use for home care patients with high medication regimen complexity: a randomized trial		It did not relate medication regiment complexity with health outcomes		
Metz et al., 2014	Patient-Level Medication Regimen Complexity in Patients With HIV	The Annals of Pharmacotherapy	The study did not evaluate health outcomes. It evaluated MRCI in Patients with HIV		
Moczygemba et al., 2011	Impact of telephone medication therapy management on medication and health-related problems, medication adherence, and medicare part D drug costs: A 6-month follow up	American Journal Geriatric Pharmacotherapy	It did not use the MRCI to measure medication regimen complexity		

Author	Title	Journal	Reason for exclusion
Morello et al., 2016	Clinical Outcomes Associated With a Collaborative Pharmacist-Endocrinologist Diabetes Intense Medical Management "Tune Up" Clinic in Complex Patients	The Annals of Pharmacotherapy	It did not relate medication regimen complexity with health outcomes
Obreli-neto et al., 2011	Effect of a 36-month pharmaceutical care program on pharmacotherapy adherence in elderly diabetic and hypertensive patients	International Journal of Clinical Pharmacy	It did not relate medication regimen complexity with health outcomes
Okuyan et al., 2016	Validation of the Turkish version of medication regimen complexity index among elderly patients	Journal of Evaluation in Clinical Practice	The study validated the MRCI to Turkish
Olson et al., 2014	Optimization of decision support tool using medication regimens to assess rehospitalization risks	mization of decision support tool Applied Clinical Informatics g medication regimens to assess	
Olson et al., 2014	Automation of a highrisk medication regime algorithm in a home health care population	Journal of Biomedical Informatics	It did not relate medication regimen complexity with health outcomes
Patel et al., 2016	Medication Complexity, Medication Number, and Their Relationships to Medication Discrepancies	The Annals of Pharmacotherapy	It did not relate medication regimen complexity with health outcomes, but with discrepancies
Remondi et al., 2014	Non-adherence to continuous treatment and associated factors: Prevalence and determinants in adults 40 years and older [Nãoadesão ao tratamento medicamentoso contínuo: Prevalência e determinantes em adultos de 40 anos e mais]	Cadernos de Saúde Pública	It did not use the MRCI to measure medication regimen complexity
Rose et al., 2015	Effect evaluation of an interprofessional BMC Family Practice medication therapy management approach for multimorbid patients in primary care: a cluster-randomized controlled trial in community care (West Gem study protocol)		It did not relate medication regimen complexity with health outcomes

Author	Title	Journal	Reason for exclusion  The study validated the MRCI to Spanish		
Saez de lafuente et al., 2016	Cross-cultural Adaptation and Validation of the Medication Regimen Complexity Index Adapted to Spanish	The Annals of Pharmacotherapy			
Serper et al., 2013	Quantifying medication regimen complexity in liver transplantation	Hepatology	The study was a publication at conferences		
Stange et al., 2012	Development and psychometric evaluation of the German version of the Medication Regimen Complexity Index (MRCI-D)	Journal of Evaluation in Clinical Practice	The study developed and validated the MRCI to German		
Stange et al., 2013	Reducing cardiovascular medication complexity in a German university hospital: effects of a structured pharmaceutical management intervention on adherence	Journal of Managed Care Pharmacy	It did not relate medication regimen complexity with health outcomes		
Sun et al., 2017	Association between use of traditional Chinese medicine and medication adherence among Chinese-American rheumatology patients	Annals of the Rheumatic Diseases	Abstract published in scientific journal		
Vries et al., 2014	Medication beliefs, treatment complexity, and non-adherence to different drug classes in patients with type 2 diabetes	Journal of Psychosomatic Research	It did not use the MRCI to measure medication regimen complexity		
Wimmer et al., 2015	Medication regimen complexity in older people with and without medication-administration problems: A nested casecontrol study	International Journal of Clinical Pharmacy	The study was a publication at conferences		

Abbreviation: MRCI - Medication Regimen Complexity Index.

APPENDIX 4 - Quality assessment of cohort studies by NOS

Author			Comparability	Outcome						
	Study design	Representativeness of the Exposed Cohort	Selection of the Non- Exposed Cohort	Ascertainment of Exposure	Demonstration That Outcome of Interest Was Not Present at Start of Study	Based on design or analysis	Assessment of Outcome	Was Follow-Up Long Enough for Outcomes to Occur	Adequacy of Follow Up of Cohorts	Score
[32]*	Cohort	*	*	*	*	*	*	*	*	8
[33]*	Cohort	*	*	*	-	**	*	-	-	6
[34]*	Cohort	*	*	Not clear	-	*	*	*	-	5
[35]*	Cohort	Not clear	*	*	*	**	*	*	-	7
[36]*	Cohort	*	*	*	-	*	*	-	*	6
[38]*	Cohort	*	*	*	-	*	*	-	*	6
[39]*	Cohort	*	*	*	-	*	*	*	*	7
[40]*	Cohort	*	*	*	Not clear	**	-	*	-	6
[41]*	Cohort	*	*	*	Not clear	*	*	*	-	6
[42]*	Cohort	Not clear	*	*	Not clear	*	Not clear	*	-	4

Abbreviation: NOS - Newcastle-Ottawa Scale.

<sup>\*</sup> Studies that scored ≥ 6 stars were considered of good quality

APPENDIX 5 - Quality assessment of case-control studies by NOS

Author		Selection				Comparability Outcome				
	Study design	Case definition adequate?	Representativeness of the cases	Selection of Controls	Definition of Controls	Based on design or analysis	Ascertainment of Exposure	Same method of ascertainment for cases and controls	Non- Response rate	Score
[31]*	Case- control	*	*	*	-	**	*	*	*	8
[37]	Case- control	*	*	Not clear	Not clear	*	*	*	Not clear	5

Abbreviation: NOS - Newcastle-Ottawa Scale.

<sup>\*</sup> Studies that scored ≥ 6 stars were considered of good quality.