Hearing, cognition and speech perception in aging: literature evidence

Audição, cognição e percepção de fala no envelhecimento: evidências da literatura

Audición, cognición y percepción del habla en el envejecimiento: evidencias de la literatura

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Abstract

Purpose: These studies assess evidences in Literature about correlation between auditory abilities and cognitive functions on elderly. It was realized a systematic review of Literature, using articles published in the last two decades, researched in Medline, Scielo and Lilacs. It was picked prospective clinical and reviewed texts that refer to the correlation between audition and cognition. Each article was evaluated concerning to the level of evidence according to "Oxford Centre for Evidence-based Medicine Levels of evidence". It was found 38 articles among 2008 and 2012 that treated specifically aging auditory and cognitive aspects, being 11% national and 89% international. From studies about correlation and interactions between auditory abilities and cognitive abilities, 15% were about descriptive reviews of literature (level of evidence 3a); 65% were about case-control (level of evidence 3b); 3,3 % were about case-control studies with poor or not independent standard of reference (level of evidence 4); 3,3% were about validation cohort only in fragmented samples (level of evidence 3b); and finally, 10% were about validation cohort, with a good standard of reference, diagnostic criteria tested in a single clinical

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center (level of evidence 1b). Few authors evaluated the correlation between hearing and cognition with adequate methods. The recommendation grade of the most of studies reviewed was B, which represents experimental or observational studies with fewer consistencies. It was observed that there are not formal protocols to assess the cognitive and central auditory abilities. Meta-analyze is difficult to have because of the variation of methods between these studies..

Keywords: *Hearing; Aged; Auditory Perception; Cognition.*

Resumo

Objetivo: Avaliar as evidências na literatura, por meio da revisão sistemática da literatura, entre habilidades auditivas e funções cognitivas no envelhecimento. **Método:** Os artigos foram pesquisados nas bases de dados Medline, Scielo e Lilacs, e avaliados quanto ao nível de evidência de acordo com "Oxford Centre for Evidence-based Medicine Levels of evidence". **Resultados:** Foram encontrados 38 artigos entre 2008 e 2012, sendo 11% nacionais e 89% internacionais, 15% eram de cunho revisão descritiva da literatura (nível de evidência 3a), 65% eram estudos caso-controle (nível de evidencia 3b), 3,3% estudos caso-controle com padrão de referência pobre ou não independente (nível de evidência 4), 3,3% estudos coorte validado somente em amostras fragmentadas (nível de evidência 3b), 3,3% de Relato de caso (incluindo Coorte ou caso-controle de menor qualidade) e por fim, 10% estudos coorte validado, com bom padrão de referência, critério diagnóstico testado em um único centro clínico (nível de evidencia 1b). Poucos foram os autores que aplicaram uma metodologia visando avaliar e estabelecer o fator de correlação entre as duas variáveis. O grau de recomendação da maior parte dos estudos encontrados é B, ou seja, estudos experimentais ou observacionais de menor consistência. **Conclusão:** A falta de um protocolo padronizado para a avaliação das funções auditivas centrais e das funções cognitivas e a variação metodológica entre os estudos encontrados prejudica a realização de uma metanálise ou uma comparação mais precisa entre os estudos.

Palavras-chave: Audição; Idoso; Percepção Auditiva; Cognição.

Resumen

Objetivo: Evaluar la evidencia en la literatura mediante la revisión sistemática de la literatura entre el auditorio y la función cognitiva en el envejecimiento. Método: Se realizaron búsquedas en los artículos en Medline, Lilacs y SciELO, y evaluaron el nivel de evidencia según el "Centro de Oxford para los niveles de Medicina Basada en Evidencia de la evidencia." Resultados: 38 artículos fueron encontrados entre 2008 y 2012, 11% internacionales interno y el 89%, 15% eran impronta revisión descriptiva de la bibliografía (nivel de evidencia 3 bis), el 65% fueron estudios de casos y controles (nivel de evidencia 3b), 3,3% de casos y controles con estándar de referência pobre o no independiente (nivel de evidencia 4), 3,3% estudios de cohortes validado sólo en muestras fragmentadas (nivel de evidencia 3b), el 3,3% de reporte de caso (incluyendo cohortes o de casos y controles de baja calidad) y, finalmente, 10% estudios de cohortes validados con buenos criterios de diagnóstico estándar de referencia probados en un único centro clínico (nivel de evidencia 1b). Pocos autores han aplicado una metodología para evaluar y establecer el factor de correlación entre las dos variables. El grado de recomendación para la mayoría de los estudios encontrados es B, es decir, estudios experimentales y observacionales de menor consistencia. Conclusión: la falta de un protocolo normalizado para la evaluación de la función auditiva central y las funciones cognitivas y la variación metodológica entre los estudios se han encontrado impedir la aplicación de un meta-análisis o una comparación más precisa entre los estudios..

Palabras clave: *Audición; Anciano; Percepción Auditiva; Cognición.*

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Introduction

The percentage of the population with communication disorders progressively increase with age. Thus, hearing loss has an adverse effect on the quality of life, the functional state, the cognitive function, and the emotional, behavioral, and social well-being of elderly individuals[1,2,3].

Presbycusis is the denomination of the process that, besides old age, has as inherent characteristic the lowering of auditory thresholds in both ears, along with a decrease in speech discrimination and in the central auditory function, which is observed by difficulties in the abilities of binaural fusion, figure-ground, selective attention, judgment of acoustic patterns, and reduction in the speed of auditory synthesis and closure[1,3].

Temporal auditory processing includes synchrony or periodical differentialencoding, duration encoding (start and end of detection), and rhythmic pattern encoding (syllabic prosody)[4,5]. With aging, the temporal auditory processing may present problems related to the discrimination of some phonemic contrasts and differences, or of vocal qualities, but not to the perception of rhythm[4,5].Hence, the aging process hinders mostly the segmental speech processing, rather than the suprasegmental[5,6,7].

One of the characteristics of central auditory aging seems to be the loss of synchrony that affects time-dependent processes necessary for binaural comparisons for the extraction of signals from noise, and for the detection of monoauralintervals[8,9]. The cognitive processes are responsible for improving the perception and allowing the comprehension of the discourse meaning, as well as for storing the information in memory and using it[8,9,10]. The reduction of white matter in the brain has also been mentioned as a possible explanation to the cognitive decline related to aging, however, the specific role of the regions where the cognitive decline occurs is still uncertain.

There are three underlying mechanisms to speech comprehension in elderly individuals: peripheral auditory aging, central auditory functions, and cognitive functions[10]. The meaning of what was heard must be adequately interpreted within the context of the social and physical environment. The correct interpretation of the message demands intentional, directed and focused attention from the listener. Cognitive factors (memory and selective attention) certainly have an important role in comprehension. Individuals with reduced memory capacity would be able to store less information during speech recognition, implicating in difficulties analyzing linguistic structures, when compared to individuals with greater storing capacity and better working memory[11,12].

When the aim is to understand speech, the listener's priority, in the process, is the perception, thus, in adverse conditions or in the presence of noise, the storage of information is reduced, intensifying the memory load by adding more information to be retrieved. Therefore, the listener – whether young or elderly – will retrieve with less effort words heard in silent environments, rather than words heard in noisy environments. However, if there is not enough information stored, the comprehension will be affected, because the accumulated information will not be exactly integrated with previous knowledge[13,14,15].

The assessment of temporal auditory processing clarifies some of the speech perception problems related to aging. Specifically, the auditory processing decline influences the ability to identify words, even out of interaction or binaural integration conditions. On the other hand, the temporal decline in the cognitive processinfluences the coordination of information in conditions of interactive or prolonged discourse[16,17,18].

Along the aging process, speech discrimination may be affected by changes in the processing, temporal and frequency resolution capacities, and in auditory sensitivity, especially in environments with competitive noise or reverberation. Thus, difficulties in speech discrimination occurs with aging, regardless of the existence of peripheral hearing loss or the use of devices for hearing rehabilitationTherefore, the elderly need better acoustic conditions than young individuals in order to accurately indentify words, even when they have hearing thresholds within normal limits.[18,19,20,21]

The use of hearing aids is recommended in hearing rehabilitation, especially in the case of elderly individuals with presbycusis. However, in some cases, the elderly report difficulties in using them, and prefer to abandon the use or make the option for unilateral adaptation, even individuals with bilateral hearing loss. Another important factor for the selection and adaptation of hearing aids is the presence of central auditory processing disorders, which may have a negative impact on this process. Nevertheless, physiological changes

in central auditory processing may be stimulated, even after hearing aid adaptation [21, 22, 23]

There are cases in which patients have no gain with binaural amplification, characterizing a binaural interference, that is, when the speech perception abilities are worse in one of the ears. Binaural interference occurs in 8 to 10% of the elderly population[24,25].Therefore, complementary tests are recommended in the amplification process, in order to verify whether there is binaural interference[26,27].

The working memory decline and the auditory processing decrease, which are characteristic of the aging process, are changes that increase the speech comprehension difficulties. Thus, it is necessary to determine hearing rehabilitation strategies.

Accordingly, the models of study for the assessment of these variables in the performance of adult hearing aid users must consider both the central auditory processing components and the cognitive abilities involved in speech comprehension[23]. Studying the auditory processing and cognitive abilities in elderly individuals and assessing the possible differences in comparison with young adults may help to adequate the protocols for hearing aid adaptation, consequently reducing the complaints and improving the qualities of hearing and of life of these individuals[28,29]. Nevertheless, for these new conducts to be adopted and recommended, it is essential to search literature for evidence on the subject.If no strong evidence or studies with high grade of recommendation are found demonstrating the association between cognitive and auditory abilities in speech perception or in the implications of this process to hearing rehabilitation in the aging process, further studies, with better designed methods should be conducted before any changes in clinical practice.

The evidence-based practice focuses on evidence classification systems, hierarchically characterized according to the methodological approach adopted in the study.Knowing these classification systems provide information to help the critical assessment of research outcomes and the decisions regarding the incorporation of these evidences into clinical practice[30].

Hence, this study had the aim to evaluate literature evidence regarding the correlation between speech perception, auditory abilities, and cognitive functions in the aging process.

Material and Methods

A systematic literature review was conducted. The databases Medline, Scielo and Lilacs were searched during the period from October 2008 to December 2012 for articles published in the last two decades, using the following English and Portuguese keywords: "Auditory perception and aged", combined with the terms "Cognition", "Elderly", "Hearing loss", and "Hearing disorders" (respectively, "Percepção auditiva e idoso", "Cognição", "Envelhecimento", "Perda auditiva", e "Transtornos da audição").

The search selected manuscripts written in English or Portuguese, regarding prospective clinical studies (cross-sectional or cohort) and literature reviews about the correlations between hearing and cognition. The articles were evaluated regarding the levels of evidence, according to the "Oxford Centre for Evidence-based Medicine Levels of evidence"[17]
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Results

During the search period, between 2008 and 2012, 38 studies were found – 11% national and 89% international. From the studies retrieved, 15% were descriptive literature reviews (level of evidence 3a), 65% were case-control studies (level of evidence 3b), 3.3% were case-control studies with poor or not independent reference standard (level of evidence 4), 3.3% were cohort studies validated only in fragmented samples (level of evidence 3b), 3.3% were case reports (including cohort or case--control studies of lower quality), and finally, 10% were validated cohort studies with good reference standard and diagnostic criteria tested in a single clinical center (level of evidence 1b). maneira isso ocorre ou o quanto essas variáveis estão fortemente correlacionadas, mas puderam mostrar que, quando comparado ao grupo controle proposto, houve diferença no desempenho de tarefas de processamento auditivo e de processamento cognitivo entre idosos e jovens, independente do grau de perda auditiva (Gráfico 1).
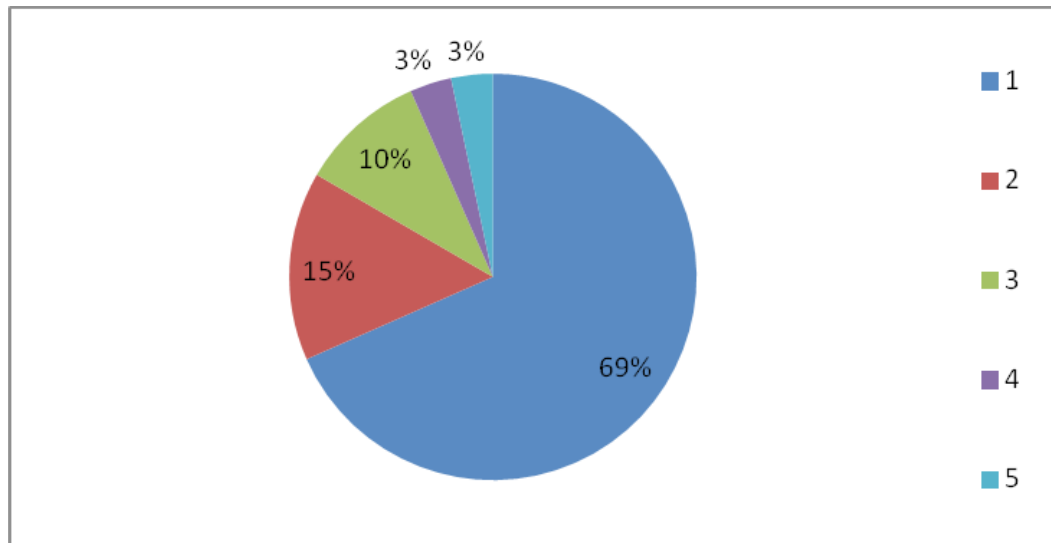
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Figure 1 – Types of studies (in percentage) that researched the interactions between cognitive and auditory functions in the normal aging process (Appendixes I and II).

Note:

		Levelofevidence
1.	Case-controlstudy	3b
2.	Systematic review (with homogeneity) of case-control studies	3a
3.	Case reports (including cohort or case-control studies with lower quality)	2b
4.	Cohort studies (contemporary or prospective) with few losses	1b
5.	Cohort studies (including randomized clinical trials of lower quality)	4

Discussion

This study had the aim to perform a literature review describing the aspects involved in the aging process and their correlation with speech perception, auditory abilities, and cognitive functions. Therefore, the importance of the study is that it leads to rethinking strategies used for audiological diagnosis and for the rehabilitation of hearing disorders, emphasizing activities that prioritize both auditory abilities and cognitive functions. Moreover, since the cognitive system seems to be associated to the auditory performance for speech recognition and the auditory processing tests could favor the selection and adaptation of hearing aids, it is necessary to investigate, primarily, the information sources, the methodologies used, and the levels of evidence of the studies on the theme.

The Oxford Centre for Evidence-Based Medicine Levels of Evidence26 presents a

methodology that allows the evaluation of the strength of the scientific evidence of a research. The classification proposed is based on the procedure used in evidence generation. The practice of evidence-based medicine (EBM) means integrating each specialty with the best possible clinical evidence provided by systematic investigation. The evidence-based practice (EBP) comprise the same concepts and principles of the EBM, but used by different professionals in several health contexts.

Only one prospective cohort study presented few losses regarding the correlations between hearing and cognition – the one from Pouchain13, from 2007. This type of study have a higher level of evidence (1B), and was the only manuscript found with grade of recommendation A. In this last study, the authors found a significant correlation between hearing loss and cognitive function in elderly over 75 years of age, regardless of gender or age. It was the study with higher sample of

subjects, including 337 patients, and the only one that traced the relative risk analysis, showing that individuals with hearing loss are 2.48 times more likely to develop cognitive deficits (CI95% = 1.54-3.99, p<0.0001). No other studies were found with similar methodology.

The remaining manuscripts presented cross-sectional (observational) or case-control studies, with grade of recommendation between B and C, as mentioned. In these studies, most authors compared the effects that different noise conditions had on cognitive performance and on language processing. Some of them correlated these effects with the hearing aid adaptation. The methods used in most of these manuscripts were not conclusive enough to safely determine if there is a decrease in auditory processing and cognition with age and how this occurs, or how strongly these variables are correlated. However, they did show that, when compared to a control group, the performance of elderly individuals in auditory and cognitive processing tasks was different from younger subjects, regardless the degree of the hearing loss (Figure 1).

Conclusion

Although the grade of recommendation of most of the studies assessed was low and the conduction of a meta-analysis was difficult due to the methodological differences between them, the theme of our study is essential and have important repercussions for clinical practice, since the analyses of these manuscripts have the main objective to propose therapeutic guidelines for a better and more consistent theoretical basis.

For stronger evidence, more cohort studies are needed. These studies should present strength and association measures between auditory and cognitive variables, and small confidence intervals. Moreover, the population should be followed-up for a longer period, in order to verify if correlation would increase with the aging process.

A meta-analysis would be of great value for scientific knowledge (grade of recommendation A). A quantitative and descriptive meta-analysis would allow better quantification of the investigation tendencies in literature through the combination of the results found. However, the methods used in the studies are different, hindering the combination and grouping of subjects.

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References

1. Baraldi GS, Almeida LC, Borges ACC. Evolução da perda auditiva no decorrer do envelhecimento. Rev. Bras. Otorrinolaringol. 2007;73(1):64-70.
2. Chisolm TH, Willott, JF, Lister, JJ. The aging auditory system: anatomic and physiologic changes and implications for rehabilitation. Int J Audiol. 2003;42: 3-10.
3. Carter, AS, Wilson, RH. Lexical effects in dichotic word recognition in young and elderly listeners. J Am Acad Audiol. 2001;12(2): 86-100,
4. Pichora-Füller MK. Hearing and Cognition: What Audiologists Need to Know about Listening. Hearing Care For Adults. Chicago, Illinois (EUA):2006;6:13-5.
5. Silveira KMM, Borges ACLC, Pereira LD. Memória, interação e integração em adultos e idosos de diferentes níveis ocupacionais, avaliados pelos testes da avaliação simplificada e teste dicótico de dígitos. Distúrb. comun. 2004;16(3):313-22.
6. Pichora-Füller MK, Souza PE. Effects of aging on auditory processing of speech. Int J Audiol. 2003;42:11-6.
7. Pichora-Füller MK. Processing speed and timing in aging adults: psychoacoustics, speech perception, and comprehension. Int J Audiol. 2003b; 42:59-67.
8. Pinheiro MMC, Pereira LD. Processamento auditivo em idosos: estudo da interação por meio de testes co estímulos verbais e não-verbais. Rev Bras Otorrinolaringol. 2004;70(2):209-14.
9. Colom R, Flores-Mendonza CE. Armazenamento de curto prazo e velocidade de processamento explicam a relação entre memória de trabalho e fator g de inteligência. Psicologia: Teoria e Pesquisa. 2006;22(1):113-22.
10. Humes LE. Aging and speech communication. The ASHA Leader, 2008;13(5):10-3.
11. Oxford Centre for Evidence-based Medicine Levels of Evidence. 2001. Disponível em : <http:/cebm.jr2.ox.ac.uk/docs/levels.html>. Acesso em: 20 dez.2013.
12. Perrella ACM, Branco-Barreiro FCA. Avaliação da função auditiva central em idosos e suas contribuições para a adaptação de próteses auditivas. Distúrb. com. 2005;17(3):333-46.
13. Pichora-Füller MK. Cognitive aging and auditory information processing. Int J Audiol. 2003a; 4: 26-32.
14. Wong PC. Aging and cortical mechanisms of speech perception in noise. Neuropsychologia. 2009;47(3): 693-703.
15. Wingfield A, Lindfield KC, Goodglass H. Effects of age and hearing sensitivity on the use of prosodic information in spoken word recognition. J Am Acad Audiol. 2000;7: 915-25.
16. Lin FR. Hearing loss and cognition among older adults in the United States. Journal of Gerontology: Medical Sciences. 2011;66:1131–6.
17. Miranda ECM, Gil D, Iório CM. Treinamento auditivo formal em idosos usuários de próteses auditivas. Rev Bras Otorrinolaringol. 2008;74(6): 919-25.
18. Commodari E, Guarnera M. Attention and aging. Aging Clin Exp Res. 2008;20(6):578-84.
19. Fogerty D, Humes LE, Kewley-Port D. Auditory temporal-order processing of vowel sequences by young and elderly listeners. J Acoust Soc Am. 2010;127:2509–20.
20. Lin FR, Ferrucci L, Metter EJ, An Y, Zonderman AB, Resnick SM. Hearing Loss and Cognition in the Baltimore Longitudinal Study of Aging Neuropsychology. Author manuscript; available in PMC 2012 November. 2011;25(6):763–70.
21. Galvão CM. Níveis de Evidência. Acta paul. enferm. 2006;19(2):5.
22. Hällgren M. Cognitive effects in dichotic speech testing in elderly persons. Ear Hear. 2001;22(2):120-9.

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23.Pouchain D. La presbyacousie est-elle un facteur de ris-

que de démence? Etude AcouDem. La Revue de gériatrie.

2007;32(6):439-45.

24.Jerger J. The complexities of research in aging. J Am Acad

Audiol. 2006;17(4):230-40.

25.Kennedy KM; Raz N. Aging white matter and cognition:

Differential effects of regional variations in diffusion properties

on memory, executive functions, and speed. Neuropsychologia.

2009;47(3):916-27.

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Appendix I

Oxford Centre for Evidence-Based Medicine Levels of Evidence (May 2001)

Produced by Bob Phillips, Chris Ball, Dave Sackett, Doug Badenoch, Sharon Straus, Brian Haynes, Martin Dawessince November 1998.

Level	Therapy/Pre-vention, Aetio-logy/Harm	Prognosis	Diagnosis	Differential diagnosis/ symptom pre-valence study	Economic and decision analy-ses
1a	SR (with ho-mogeneity*) of RCTs	SR (with ho-mogeneity*) of inception cohort studies; CDR† valida-ted in different populations	SR (with homoge-neity*) of Level 1 diagnostic studies; CDR† with 1b stu-dies from different clinical centres	SR (with ho-mogeneity*) of prospective cohort studies	SR (with ho-mogeneity*) of Level 1 eco-nomic studies
1b	Individual RCT (with narrow Confidence In-terval‡)	Individual in-ception cohort study with > 80% follow--up; CDR† validated in a single popu-lation	Validating** co-hort study with good††† referen-ce standards; or CDR† tested within one clinical centre	Prospective cohort study with good follow-up****	Analysis based on clinically sensible costs or alternati-ves; systema-tic review(s) of the eviden-ce; and inclu-ding multi-way sensitivity analyses
1c	All or none§	All or none case-series	Absolute SpPins and SnNouts††	All or none case-series	Absolute better-value or worse-value analyses ††††
2a	SR (with ho-mogeneity*) of cohort stu-dies	SR (with ho-mogeneity*) of either re-trospective cohort studies or untreated control groups in RCTs	SR (with homoge-neity*) of Level >2 diagnostic studies	SR (with ho-mogeneity*) of 2b and bet-ter studies	SR (with ho-mogeneity*) of Level >2 economic stu-dies
2b	Individual cohort study (including low quality RCT; e.g., <80% follow-up)	Retrospective cohort study or follow-up of untreated con-trol patients in an RCT; Deri-vation of CDR† or validated on split-sam-ple§§§ only	Exploratory** cohort study with good†††reference standards; CDR† after derivation, or validated only on split-sample§§§ or databases	Retrospective cohort study, or poor follow--up	Analysis based on clinically sensible costs or alternati-ves; limited review(s) of the eviden-ce, or single studies; and including mul-ti-way sensiti-vity analyses
2c	"Outcomes" Research; Ecological stu-dies	"Outcomes" Research		Ecological stu-dies	Audit or outco-mes research

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3a	SR (with ho-mogeneity*) of case-control studies		SR (with homoge-neity*) of 3b and better studies	SR (with ho-mogeneity*) of 3b and bet-ter studies	SR (with ho-mogeneity*) of 3b and bet-ter studies
3b	Individual Case-Control Study		Non-consecutive study; or without consistently ap-plied reference standards	Non-conse-cutive cohort study, or very limited popu-lation	Analysis ba-sed on limited alternatives or costs, poor quality esti-mates of data, but including sensitivity analyses in-corporating clinically sen-sible varia-tions.
4	Case-series (and poor quality cohort and case-con-trol studies§§)	Case-series (and poor quality prog-nostic cohort studies***)	Case-control stu-dy, poor or non--independent refe-rence standard	Case-series or superse-ded reference standards	Analysis with no sensitivity analysis
5	Expert opi-nion without explicit critical appraisal, or based on phy-siology, bench research or "first princi-ples"	Expert opi-nion without explicit critical appraisal, or based on phy-siology, bench research or "first princi-ples"	Expert opinion wi-thout explicit cri-tical appraisal, or based on physiolo-gy, bench research or "first principles"	Expert opi-nion without explicit critical appraisal, or based on phy-siology, bench research or "first principles	Expert opi-nion without explicit critical appraisal, or based on eco-nomic theory or "first princi-ples"

Notes

Users can add a minus-sign "-" to denote the level of that fails to provide a conclusive answer because of:

•EITHER a single result with a wide Confidence Interval (such that, for example, an ARR in an RCT is not statistically significant but whose confidence intervals fail to exclude clinically important benefit or harm)

•OR a Systematic Review with troublesome (and statistically significant) heterogeneity.

•Such evidence is inconclusive, and therefore can only generate Grade D recommendations.

*	By homogeneity we mean a systematic review that is free of worrisome variations (heteroge-neity) in the directions and degrees of results between individual studies. Not all systematic reviews with statistically significant heterogeneity need be worrisome, and not all worrisome heterogeneity need be statistically significant. As noted above, studies displaying worrisome heterogeneity should be tagged with a "-" at the end of their designated level.
†	Clinical Decision Rule. (These are algorithms or scoring systems which lead to a prognostic estimation or a diagnostic category.)
‡	See note #2 for advice on how to understand, rate and use trials or other studies with wide confidence intervals.
§	Met when all patients died before the Rx became available, but some now survive on it; or when some patients died before the Rx became available, but none now die on it.

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§§	By poor quality cohort study we mean one that failed to clearly define comparison groups and/or failed to measure exposures and outcomes in the same (preferably blinded), objective way in both exposed and non-exposed individuals and/or failed to identify or appropriately control known confounders and/or failed to carry out a sufficiently long and complete follow-up of patients. By poor quality case-control study we mean one that failed to clearly define comparison groups and/or failed to measure exposures and outcomes in the same (preferably blinded), objective way in both cases and controls and/or failed to identify or appropriately control known confounders.
§§§	Split-sample validation is achieved by collecting all the information in a single tranche, then artificially dividing this into "derivation" and "validation" samples.
††	An "Absolute SpPin" is a diagnostic finding whose Specificity is so high that a Positive result rules-in the diagnosis. An "Absolute SnNout" is a diagnostic finding whose Sensitivity is so high that a Negative result rules-out the diagnosis.
‡‡	Good, better, bad and worse refer to the comparisons between treatments in terms of their clinical risks and benefits.
†††	Good reference standards are independent of the test, and applied blindly or objectively to applied to all patients. Poor reference standards are haphazardly applied, but still independent of the test. Use of a non-independent reference standard (where the 'test' is included in the 'reference', or where the 'testing' affects the 'reference') implies a level 4 study.
††††	Better-value treatments are clearly as good but cheaper, or better at the same or reduced cost. Worse-value treatments are as good and more expensive, or worse and the equally or more expensive.
**	Validating studies test the quality of a specific diagnostic test, based on prior evidence. An exploratory study collects information and trawls the data (e.g. using a regression analysis) to find which factors are 'significant'.
***	By poor quality prognostic cohort study we mean one in which sampling was biased in favour of patients who already had the target outcome, or the measurement of outcomes was accomplished in <80% of study patients, or outcomes were determined in an unblinded, non-objective way, or there was no correction for confounding factors.
****	Good follow-up in a differential diagnosis study is >80%, with adequate time for alternative diagnoses to emerge (eg 1-6 months acute, 1 - 5 years chronic)

Grades of Recommendation

A	consistent level 1 studies
B	consistent level 2 or 3 studies or extrapolations from level 1 studies
C	level 4 studies or extrapolations from level 2 or 3 studies
D	level 5 evidence or troublingly inconsistent or inconclusive studies of any level

"Extrapolations" are where data is used in a situation which has potentially clinically important differences than the original study situation.

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Anexo II

Nível de Evidência Científica por Tipo de Estudo - "Oxford Centre for Evidence-based Medicine" - última atualização maio de 2001

Grau de Recomendação	Nível de Evidência	Tratamento/ Prevenção – Etiologia	Prognóstico	Diagnóstico	Diagnóstico Diferencial/ Prevalência de Sintomas
A	1A	Revisão Sistemática (com homogeneidade) de Ensaios Clínicos Controlados e Randomizados	Revisão Sistemática (com homogeneidade) de Coortes desde o início da doença Critério Prognóstico validado em diversas populações	Revisão Sistemática (com homogeneidade) de Estudos Diagnósticos nível 1 Critério Diagnóstico de estudos nível 1B, em diferentes centros clínicos	Revisão Sistemática (com homogeneidade) de Estudo de Coorte (contemporânea ou prospectiva)
	1B	Ensaio Clínico Controlado e Randomizado com Intervalo de Confiança Estreito	Coorte, desde o início da doença, com perda < 20% Critério Prognóstico validado em uma única população	Coorte validada, com bom padrão de referência Critério Diagnóstico testado em um único centro clínico	Estudo de Coorte (contemporânea ou prospectiva) com poucas perdas
	1C	Resultados Terapêuticos do tipo "tudo ou nada"	Série de Casos do tipo "tudo ou nada"	Sensibilidade e Especificidade próximas de 100%	Série de Casos do tipo "tudo ou nada

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B	2A	Revisão Sistemática (com homogeneidade) de Estudos de Coorte	Revisão Sistemática (com homogeneidade) de Coortes históricas (retrospectivas) ou de seguimento de casos não tratados de grupo controle de ensaio clínico randomizado	Revisão Sistemática (com homogeneidade) de estudos diagnósticos de nível > 2	Revisão Sistemática (com homogeneidade) de estudos sobre diagnóstico diferencial de nível > 2b
	2B	Estudo de Coorte (incluindo Ensaio Clínico Randomizado de Menor Qualidade)	Estudo de coorte histórica Seguimento de pacientes não tratados de grupo controle de ensaio clínico randomizado Critério Prognóstico derivado ou validado somente em amostras fragmentadas	Coorte Exploratória com bom padrão de referência Critério Diagnóstico derivado ou validado em amostras fragmentadas ou banco de dados	Estudo de coorte histórica (coorte retrospectiva) ou com seguimento de casos comprometido (número grande de perdas)
	2C	Observação de Resultados Terapêuticos (outcomes research) Estudo Ecológico	Observação de Evoluções Clínicas (outcomes research)		Estudo Ecológico
	3A	Revisão Sistemática (com homogeneidade) de Estudos Caso-Controle		Revisão Sistemática (com homogeneidade) de estudos diagnósticos de nível > 3B	Revisão Sistemática (com homogeneidade) de estudos de nível > 3B
	3B	Estudo Caso-Controle		Seleção não consecutiva de casos, ou padrão de referência aplicado de forma pouco consistente	Coorte com seleção não consecutiva de casos, ou população de estudo muito limitada
c	4	Relato de Casos (incluindo Coorte ou Caso-Controle de menor qualidade)	Série de Casos (e coorte prognóstica de menor qualidade)	Estudo caso-controle; ou padrão de referência pobre ou não independente	Série de Casos, ou padrão de referência superado
D	5	Opinião desprovida de avaliação crítica ou baseada em matérias básicas (estudo fisiológico ou estudo com animais)			