

## **Appendix A: Literature Search Strategy**

Databases: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <March 09, 2011>, EBM Reviews - Cochrane Database of Systematic Reviews <2005 to February 2011>, EBM Reviews - Cochrane Central Register of Controlled Trials <1st Quarter 2011>, Ovid MEDLINE(R) without Revisions <1996 to March Week 1 2011>

Last run 3/11/2011

- 1 Immunoglobulin Light Chain\*.mp. or exp Immunoglobulin Light Chains/ (4166)
- 2 monoclonal light chain\*.mp. (126)
- 3 serum free light chain\*.mp. (145)
- 4 immunoglobulin-free light chain\*.mp. (61)
- 5 Bence Jones protein.mp. or exp Bence Jones Protein/ (353)
- 6 1 or 2 or 3 or 4 or 5 (4498)
- 7 limit 6 to english language [Limit not valid in CDSR,CCTR; records were retained] (4070)
- 8 limit 7 to yr="2000 -Current" (2826)
- 9 remove duplicates from 8 (2819)

## Appendix B: Excluded Studies

Of the 290 articles obtained for full-text screening, 13 were included and 277 were excluded (see first list below). Of the excluded studies, 236 were excluded during full-text screening, for one of four main reasons: not relevant (or insufficient information) re test, population, diagnosis, or comparison; narrative review or commentary; single case series; and letter without data.

The remaining 41 studies required in-depth review before being rejected because they did not meet one or more of the PICO (population, intervention, comparator, and outcome) criteria for a particular Key Question (see second list below).

All the excluded references are presented in the two lists below, both in alphabetic order of first author's surname, along with the reason for exclusion for each. The first list comprises the 236 initially excluded articles; the second list, the 41 articles excluded only after full-text review.

### Studies Excluded after Full-Text Screening (n=236)

1. Adamczyk M, Gebler JC, Wu J. Profiling of polyclonal antibody light chains by liquid chromatography/electrospray ionization mass spectrometry. *Rapid Communications in Mass Spectrometry* 2000;14(1):49-51. *Not relevant re test, population, diagnosis, or comparison.*
2. Alpay N, Artim-Esen B, Kamali S, et al. Amyloid arthropathy mimicking seronegative rheumatoid arthritis in multiple myeloma: case reports and review of the literature. [Review] [23 refs]. *Amyloid* 2009 Dec;16(4):226-31. *Not relevant re test, population, diagnosis, or comparison.*
3. Alyanakian MA, Abbas A, Delarue R, et al. Free immunoglobulin light-chain serum levels in the follow-up of patients with monoclonal gammopathies: correlation with 24-hr urinary light-chain excretion. *American Journal of Hematology* 2004 Apr;75(4):246-48. *Not relevant re test, population, diagnosis, or comparison.*
4. Amersdorfer P, Marks JD. Phage libraries for generation of anti-botulinum scFv antibodies. *Methods in Molecular Biology* 2000;145:219-40. *Not relevant re test, population, diagnosis, or comparison.*
5. Anagnostopoulos A, Galani E, Gika D, et al. Monoclonal gammopathy of undetermined significance (MGUS) in patients with solid tumors: effects of chemotherapy on the monoclonal protein. *Annals of Hematology* 2004 Oct;83(10):658-60. *Not relevant re test, population, diagnosis, or comparison.*
6. Anagnostopoulos A, Hamilos G, Zorzou MP, et al. Discordant response or progression in patients with myeloma treated with thalidomide-based regimens. *Leukemia & Lymphoma* 2004 Jan;45(1):113-16. *Not relevant re test, population, diagnosis, or comparison.*
7. Anand M, Singh S, Kumar R, et al. Value of immunofixation on serum in light-chain myeloma. *Annals of Clinical Biochemistry* 2004 Nov;41(Pt:6):6-2. *Not relevant re test, population, diagnosis, or comparison.*
8. Ansari NA, Owais M, Usha. Immunoglobulin heavy and light chain isotypes in multiple myeloma patients. *Asian Pacific Journal of Cancer Prevention: Apjcp* 2007 Oct;8(4):593-96. *Not relevant re test, population, diagnosis, or comparison.*

9. Artero S, Lefranc MP. The telostei immunoglobulin light IGL1 and IGL2 V, J and C genes. *Experimental & Clinical Immunogenetics* 2000;17(3):162-72.  
*Not relevant re test, population, diagnosis, or comparison.*
10. Attaelmannan M, Levinson SS. Understanding and identifying monoclonal gammopathies. [Review] [58 refs]. *Clin Chem* 2000 Aug;46(8:Pt 2):t-8.  
*Narrative review or commentary.*
11. Ayliffe MJ, Davies FE, de CD, et al. Demonstration of changes in plasma cell subsets in multiple myeloma. *Haematologica* 2007 Aug;92(8):1135-38.  
*Not relevant re test, population, diagnosis, or comparison.*
12. Bakker AJ, Bierma-Ram A, Elderman-van der WC, et al. Quantitation of serum free light chains. *Clin Chem* 2009;55(8):1585-87.  
*Letter without data.*
13. Bakshi NA, Gulbranson R, Garstka D, et al. Serum free light chain (FLC) measurement can aid capillary zone electrophoresis in detecting subtle FLC-producing M proteins. *American Journal of Clinical Pathology* 2005 Aug;124(2):214-18.  
*Not relevant re test, population, diagnosis, or comparison.*
14. Barraclough KA, Dowling JP, Schwarzer AP, et al. Sequential autologous peripheral blood stem cell transplantation and kidney transplantaion of light chain deposition disease. *Nephrology Dialysis Transplantation* 2007 Apr;22(4):1268-69.  
*Study of single case.*
15. Bartels H, Dikkers FG, van der Wal JE, et al. Laryngeal amyloidosis: localized versus systemic disease and update on diagnosis and therapy. *Annals of Otology, Rhinology & Laryngology* 2004 Sep;113(9):741-48.  
*Not relevant re test, population, diagnosis, or comparison.*
16. Bayer-Garner IB, Prieto VG, Smoller BR. Detection of clonality with kappa and lambda immunohistochemical analysis in cutaneous plasmacytomas. *Archives of Pathology & Laboratory Medicine* 2004 Jun;128(6):645-48.  
*Not relevant re test, population, diagnosis, or comparison.*
17. Beers R, Chowdhury P, Bigner D, et al. Immunotoxins with increased activity against epidermal growth factor receptor vIII-expressing cells produced by antibody phage display. *Clinical Cancer Research* 2000 Jul;6(7):2835-43.  
*Not relevant re test, population, diagnosis, or comparison.*
18. Beetham R. Detection of Bence-Jones protein in practice. [Review] [53 refs]. *Annals of Clinical Biochemistry* 2000 Sep;37(Pt 5):563-70.  
*Narrative review or commentary.*
19. Bergon E, Miravalles E, Bergon E, et al. The predictive power of serum kappa/lambda ratios for discrimination between monoclonal gammopathy of undetermined significance and multiple myeloma.[Erratum appears in *Clin Chem Lab Med*. 2005;43(3):349]. *Clinical Chemistry & Laboratory Medicine* 2005;43(1):32-37.  
*Not relevant re test, population, diagnosis, or comparison.*
20. Bergon E, Miravalles E. Estimation of serum M-protein concentration from polyclonal immunoglobulins: an alternative to serum protein electrophoresis and standard immunochemical procedures. *Clinical Chemistry & Laboratory Medicine* 2008;46(8):1156-62.  
*Not relevant re test, population, diagnosis, or comparison.*
21. Blade J. Clinical practice. Monoclonal gammopathy of undetermined significance. [Review] [31 refs]. *New England Journal of Medicine* 2006 Dec 28;355(26):2765-70.  
*Study of single case.*
22. Blade J, Rosinol L, Cibeira MT, et al. Pathogenesis and progression of monoclonal gammopathy of undetermined significance. [Review] [63 refs]. *Leukemia* 2008 Sep;22(9):1651-57.  
*Narrative review or commentary.*
23. Bosmann M, Kossler J, Stolz H, et al. Detection of serum free light chains: the problem with antigen excess. *Clinical Chemistry & Laboratory Medicine* 2010 Oct;48(10):1419-22.  
*Not relevant re test, population, diagnosis, or comparison.*

24. Bradwell AR, Carr-Smith HD, Mead GP, et al. Highly sensitive, automated immunoassay for immunoglobulin free light chains in serum and urine. *Clin Chem* 2001 Apr;47(4):673-80.  
*Not relevant re test, population, diagnosis, or comparison.*
25. Bradwell AR, Carr-Smith HD, Mead GP, et al. Serum test for assessment of patients with Bence Jones myeloma. *Lancet* 2003 Feb 8;361(9356):489-91.  
*Not relevant re test, population, diagnosis, or comparison.*
26. Briand PY, Decaux O, Caillon H, et al. Analytical performance of the serum free light chain assay. *Clinical Chemistry & Laboratory Medicine* 2010;48(1):73-79.  
*Not relevant re test, population, diagnosis, or comparison.*
27. Brunvand MW, Bitter M. Amyloidosis relapsing after autologous stem cell transplantation treated with bortezomib: normalization of detectable serum-free light chains and reversal of tissue damage with improved suitability for transplant. *Haematologica* 2010 Mar;95(3):519-21.  
*Not relevant re test, population, diagnosis, or comparison.*
28. Bui AT, Rosen BS, Roe RH, et al. Diagnostic and therapeutic challenges. *Retina* 2010 Nov;30(10):1744-48.  
*Not relevant re test, population, diagnosis, or comparison.*
29. Buxbaum JN. Abnormal immunoglobulin synthesis in monoclonal immunoglobulin light chain and light and heavy chain deposition disease. *Amyloid* 2001 Jun;8(2):84-93.  
*Not relevant re test, population, diagnosis, or comparison.*
30. Cacoub P, Camproux AC, Thiolieries JM, et al. A new approach for rapid detection and typing of serum monoclonal components. *Clinica Chimica Acta* 2000 Dec;302(1-2):105-24.  
*Not relevant re test, population, diagnosis, or comparison.*
31. Carpenter GH, Proctor GB. Double electrophoretic separation and lectin analyses of the component chains of secretory immunoglobulin A from human saliva. *Electrophoresis* 2000 May;21(8):1446-53.  
*Not relevant re test, population, diagnosis, or comparison.*
32. Charlton KA, Moyle S, Porter AJ, et al. Analysis of the diversity of a sheep antibody repertoire as revealed from a bacteriophage display library. *Journal of Immunology* 2000 Jun 15;164(12):6221-29.  
*Not relevant re test, population, diagnosis, or comparison.*
33. Cherry SR, Beard C, Jaenisch R, et al. V(D)J recombination is not activated by demethylation of the kappa locus. *Proceedings of the National Academy of Sciences of the United States of America* 2000 Jul 18;97(15):8467-72.  
*Not relevant re test, population, diagnosis, or comparison.*
34. Ching AK, Li PS, Chan WY, et al. Strand bias in Ig somatic hypermutation is determined by signal sequence within the variable region. *International Immunology* 2000 Sep;12(9):1245-53.  
*Not relevant re test, population, diagnosis, or comparison.*
35. Chiu YW, Chen R, Li QX, et al. Derivation and properties of recombinant Fab antibodies to coplanar polychlorinated biphenyls. *Journal of Agricultural & Food Chemistry* 2000 Jun;48(6):2614-24.  
*Not relevant re test, population, diagnosis, or comparison.*
36. Cohen AD, Comenzo RL. Systemic light-chain amyloidosis: advances in diagnosis, prognosis, and therapy. *Hematology* 2010;2010:287-94.  
*Narrative review or commentary.*
37. Colombat M, Mal H, Copie-Bergman C, et al. Primary cystic lung light chain deposition disease: a clinicopathologic entity derived from unmutated B cells with a stereotyped IGHV4-34/IGKV1 receptor. *Blood* 2008 Sep 1;112(5):2004-12.  
*Not relevant re test, population, diagnosis, or comparison.*

38. Condon C, Hourihane SL, ng-Lawson M, et al. Aberrant trafficking of the B cell receptor Ig-alpha beta subunit in a B lymphoma cell line. *Journal of Immunology* 2000 Aug 1;165(3):1427-37.  
*Not relevant re test, population, diagnosis, or comparison.*
39. Daval S, Tridon A, Mazon N, et al. Risk of antigen excess in serum free light chain measurements. *Clin Chem* 2007 Nov;53(11):1985-86.  
*Study of single case.*
40. Davern S, Tang LX, Williams TK, et al. Immunodiagnostic capabilities of anti-free immunoglobulin light chain monoclonal antibodies. *American Journal of Clinical Pathology* 2008 Nov;130(5):702-11.  
*Not relevant re test, population, diagnosis, or comparison.*
41. Davids MS, Murali MR, Kuter DJ. Serum free light chain analysis. [Review]. *American Journal of Hematology* 2010 Oct;85(10):787-90.  
*Narrative review or commentary.*
42. de Kat Angelino CM, Raymakers R, Teunesen MA, et al. Overestimation of serum kappa free light chain concentration by immunonephelometry. *Clin Chem* 2010 Jul;56(7):1188-90.  
*Not relevant re test, population, diagnosis, or comparison.*
43. de Larrea CF, Cibeira MT, Elena M, et al. Abnormal serum free light chain ratio in patients with multiple myeloma in complete remission has strong association with the presence of oligoclonal bands: implications for stringent complete remission definition. *Blood* 2009 Dec 3;114(24):4954-56.  
*Not relevant re test, population, diagnosis, or comparison.*
44. Dember LM. Light chains, casts, sheets and fibrils: monoclonal immunoglobulin diseases and immunotactoid/fibrillary glomerulopathy. *Clinical Journal of The American Society of Nephrology: CJASN* 2006 Nov;1(6):1320-21.  
*Narrative review or commentary.*
45. Diamantidis MD, Ioannidou-Papagiannaki E, Ntaios G. Novel extended reference range for serum kappa/lambda free light chain ratio in diagnosing monoclonal gammopathies in renal insufficient patients. *Clinical Biochemistry* 2009 Jul;42(10-11):1202-03.  
*Letter without data.*
46. Dimopoulos M, Kastritis E. High dose therapy for light chain amyloidosis: can we reduce treatment related mortality further? *Leukemia & Lymphoma* 2008 Jan;49(1):4-5.  
*Narrative review or commentary.*
47. Dingli D, Kyle RA, Rajkumar SV, et al. Immunoglobulin free light chains and solitary plasmacytoma of bone. *Blood* 2006 Sep 15;108(6):1979-83.  
*Not relevant re test, population, diagnosis, or comparison.*
48. Dispenzieri A, Kyle RA, Katzmann JA, et al. Immunoglobulin free light chain ratio is an independent risk factor for progression of smoldering (asymptomatic) multiple myeloma. *Blood* 2008 Jan 15;111(2):785-89.  
*Not relevant re test, population, diagnosis, or comparison.*
49. Dispenzieri A. Is early, deep free light chain response really an adverse prognostic factor? *Blood* 2008;111(4):2490-91.  
*Letter without data.*
50. Dispenzieri A, Kyle R, Merlini G, et al. International Myeloma Working Group guidelines for serum-free light chain analysis in multiple myeloma and related disorders. [Review] [43 refs]. *Leukemia* 2009 Feb;23(2):215-24.  
*Not relevant re test, population, diagnosis, or comparison.*
51. Dong X, An B, Salvucci KL, et al. Modification of the amino terminus of a class II epitope confers resistance to degradation by CD13 on dendritic cells and enhances presentation to T cells. *Journal of Immunology* 2000 Jan 1;164(1):129-35.  
*Not relevant re test, population, diagnosis, or comparison.*

52. Doyle A, Soutar R, Geddes CC. Multiple myeloma in chronic kidney disease. Utility of discretionary screening using serum electrophoresis. *Nephron* 2009;111(1):c7-11.  
*Not relevant re test, population, diagnosis, or comparison.*
53. Doyle ML, Brigham-Burke M, Blackburn MN, et al. Measurement of protein interaction bioenergetics: application to structural variants of anti-sCD4 antibody. *Methods in Enzymology* 2000;323:207-30.  
*Not relevant re test, population, diagnosis, or comparison.*
54. Drayson M, Tang LX, Drew R, et al. Serum free light-chain measurements for identifying and monitoring patients with nonsecretory multiple myeloma. *Blood* 2001 May 1;97(9):2900-02.  
*Not relevant re test, population, diagnosis, or comparison.*
55. Drayson M, Begum G, Basu S, et al. Effects of paraprotein heavy and light chain types and free light chain load on survival in myeloma: an analysis of patients receiving conventional-dose chemotherapy in Medical Research Council UK multiple myeloma trials. *Blood* 2006 Sep 15;108(6):2013-19.  
*Not relevant re test, population, diagnosis, or comparison.*
56. Feeney AJ. New alleles of human immunoglobulin kappa J segments IGKJ2 and IGKJ4. *Immunogenetics* 2000 May;51(6):487-88.  
*Not relevant re test, population, diagnosis, or comparison.*
57. Feld JJ, Guindi M, Heathcote EJ. The lighter side of myeloma: an easily overlooked diagnosis. *Gut* 2005;54(10):1376.  
*Not relevant re test, population, diagnosis, or comparison.*
58. Forsyth J, Hill P. Serum free light chains. *Annals of Clinical Biochemistry* 2008;45(Pt:4):4-5.  
*Letter without data.*
59. Gamba G, Montani N, Anesi E, et al. Clotting alterations in primary systemic amyloidosis. *Haematologica* 2000 Mar;85(3):289-92.  
*Not relevant re test, population, diagnosis, or comparison.*
60. Gavrilov V, Yermiahu T, Gorodischer R. Urinary excretion of retinol in patients with multiple myeloma: a preliminary study. *American Journal of Hematology* 2003 Nov;74(3):202-04.  
*Not relevant re test, population, diagnosis, or comparison.*
61. Gertz MA, Kyle RA. Amyloidosis with IgM monoclonal gammopathies. *Seminars in Oncology* 2003 Apr;30(2):325-28.  
*Not relevant re test, population, diagnosis, or comparison.*
62. Gertz MA, Blood E, Vesole DH, et al. A multicenter phase 2 trial of stem cell transplantation for immunoglobulin light-chain amyloidosis (E4A97): an Eastern Cooperative Oncology Group Study. *Bone Marrow Transplantation* 2004 Jul;34(2):149-54.  
*Not relevant re test, population, diagnosis, or comparison.*
63. Gertz MA, Lacy MQ, Dispenzieri A, et al. Amyloidosis: diagnosis and management. [Review] [103 refs]. *Clinical Lymphoma & Myeloma* 2005 Nov;6(3):208-19.  
*Narrative review or commentary.*
64. Gertz MA, Leung N, Lacy MQ, et al. Clinical outcome of immunoglobulin light chain amyloidosis affecting the kidney. *Nephrology Dialysis Transplantation* 2009 Oct;24(10):3132-37.  
*Not relevant re test, population, diagnosis, or comparison.*
65. Gokden N, Cetin N, Colakoglu N, et al. Morphologic manifestations of combined light-chain deposition disease and light-chain cast nephropathy. *Ultrastructural Pathology* 2007 Mar;31(2):141-49.  
*Not relevant re test, population, diagnosis, or comparison.*
66. Graziani MS, Merlini G. Measurement of free light chains in urine. *Clin Chem* 2001 Nov;47(11):2069-70.  
*Letter without data.*
67. Guo B, Kato RM, Garcia-Lloret M, et al. Engagement of the human pre-B cell receptor generates a lipid raft-dependent calcium signaling complex. *Immunity* 2000 Aug;13(2):243-53.  
*Not relevant re test, population, diagnosis, or comparison.*

68. Hanson BL, Bunick GJ, Harp JM, et al. Mcg in 2030: new techniques for atomic position determination of immune complexes. [Review] [29 refs]. *Journal of Molecular Recognition* 2002 Sep;15(5):297-305. *Not relevant re test, population, diagnosis, or comparison.*
69. Harding SJ, Mead GP, Bradwell AR, et al. Serum free light chain immunoassay as an adjunct to serum protein electrophoresis and immunofixation electrophoresis in the detection of multiple myeloma and other B-cell malignancies. *Clinical Chemistry & Laboratory Medicine* 2009;47(3):302-04. *Not relevant re test, population, diagnosis, or comparison.*
70. Harris DL, King E, Ramsland PA, et al. Binding of nascent collagen by amyloidogenic light chains and amyloid fibrillogenesis in monolayers of human fibrocytes. *Journal of Molecular Recognition* 2000 Jul;13(4):198-212. *Not relevant re test, population, diagnosis, or comparison.*
71. Hassoun H, Flombaum C, D'Agati VD, et al. High-dose melphalan and auto-SCT in patients with monoclonal Ig deposition disease. *Bone Marrow Transplantation* 2008 Sep;42(6):405-12. *Not relevant re test, population, diagnosis, or comparison.*
72. Hatada EN, Chen-Kiang S, Scheidereit C. Interaction and functional interference of C/EBPbeta with octamer factors in immunoglobulin gene transcription. *European Journal of Immunology* 2000 Jan;30(1):174-84. *Not relevant re test, population, diagnosis, or comparison.*
73. Hazenberg BP, van G, II, Bijzet J, et al. Diagnostic and therapeutic approach of systemic amyloidosis. [Review] [36 refs]. *Netherlands Journal of Medicine* 2004 Apr;62(4):121-28. *Narrative review or commentary.*
74. Hazenberg BP, van Rijswijk MH, Piers DA, et al. Diagnostic performance of 123I-labeled serum amyloid P component scintigraphy in patients with amyloidosis. *American Journal of Medicine* 2006 Apr;119(4):355-24. *Not relevant re test, population, diagnosis, or comparison.*
75. Herzum I, Renz H, Wahl HG. Immunochemical quantification of free light chains in urine. *Clin Chem* 2005 Jun;51(6):1033-35. *Not relevant re test, population, diagnosis, or comparison.*
76. Hiatt A, Pauly M. Monoclonal antibodies from plants: a new speed record. *Proceedings of the National Academy of Sciences of the United States of America* 2006 Oct 3;103(40):14645-46. *Narrative review or commentary.*
77. Hill PG, Forsyth JM, Rai B, et al. Serum free light chains: an alternative to the urine Bence Jones proteins screening test for monoclonal gammopathies. *Clin Chem* 2006 Sep;52(9):1743-48. *Not relevant re test, population, diagnosis, or comparison.*
78. Hopper JE, Golbus J, Meyer C, et al. Urine free light chains in SLE: clonal markers of B-cell activity and potential link to in vivo secreted Ig. *Journal of Clinical Immunology* 2000 Mar;20(2):123-37. *Not relevant re test, population, diagnosis, or comparison.*
79. Hsi ED, Hoeltge G, Tubbs RR. Biclinal chronic lymphocytic leukemia. *American Journal of Clinical Pathology* 2000 Jun;113(6):798-804. *Not relevant re test, population, diagnosis, or comparison.*
80. Hummel M, Stein H. Clinical relevance of immunoglobulin mutation analysis. [Review] [61 refs]. *Current Opinion in Oncology* 2000 Sep;12(5):395-402. *Not relevant re test, population, diagnosis, or comparison.*
81. Hussein MA, Juturi JV, Rybicki L, et al. Etanercept therapy in patients with advanced primary amyloidosis. *Medical Oncology* 2003;20(3):283-90. *Not relevant re test, population, diagnosis, or comparison.*
82. Hutchison CA, Cockwell P, Reid S, et al. Efficient removal of immunoglobulin free light chains by hemodialysis for multiple myeloma: in vitro and in vivo studies. *Journal of the American Society of Nephrology* 2007 Mar;18(3):886-95. *Not relevant re test, population, diagnosis, or comparison.*

83. Hutchison CA, Harding S, Hewins P, et al. Quantitative assessment of serum and urinary polyclonal free light chains in patients with chronic kidney disease. *Clinical Journal of The American Society of Nephrology: CJASN* 2008 Nov;3(6):1684-90.  
*Not relevant re test, population, diagnosis, or comparison.*
84. Hutchison CA. Reduction of serum free light chains predict renal recovery. *Annals of Hematology* 2010 Jun;89(6):627-28.  
*Letter without data.*
85. Iggo N, Littlewood T, Winearls CG. Prospects for effective treatment of AL amyloidosis? *Qjm* 2000 May;93(5):257-60.  
*Not relevant re test, population, diagnosis, or comparison.*
86. Invernizzi R, Palladini G, Benatti C, et al. Bone marrow amyloidosis. *Haematologica* 2006 May;91(5:Suppl):Suppl.  
*Study of single case.*
87. Itzykson R, Le Garff-Tavernier M, Katsahian S, et al. Serum-free light chain elevation is associated with a shorter time to treatment in Waldenstrom's macroglobulinemia. *Haematologica* 2008 May;93(5):793-94.  
*Not relevant re test, population, diagnosis, or comparison.*
88. Jacobs JF, Joosten I, Klasen IS. Detecting only light chains, now what? *Clin Chem* 2010 Aug;56(8):1368.  
*Not relevant re test, population, diagnosis, or comparison.*
89. Jagannath S. Value of serum free light chain testing for the diagnosis and monitoring of monoclonal gammopathies in hematology. *Clinical Lymphoma & Myeloma* 2007 Sep;7(8):518-23.  
*Narrative review or commentary.*
90. Jena PK, Liu AH, Smith DS, et al. Sequence heterogeneity in Ig kappa transcripts from single B lymphocytes. *Molecular Immunology* 2000 Apr;37(6):265-72.  
*Not relevant re test, population, diagnosis, or comparison.*
91. Kaleem Z, Zehnbauer BA, White G, et al. Lack of expression of surface immunoglobulin light chains in B-cell non-Hodgkin lymphomas. *American Journal of Clinical Pathology* 2000 Mar;113(3):399-405.  
*Not relevant re test, population, diagnosis, or comparison.*
92. Katzmman JA, Clark RJ, Abraham RS, et al. Serum reference intervals and diagnostic ranges for free kappa and free lambda immunoglobulin light chains: relative sensitivity for detection of monoclonal light chains. *Clin Chem* 2002 Sep;48(9):1437-44.  
*Not relevant re test, population, diagnosis, or comparison.*
93. Katzmman JA, Abraham RS, Dispenzieri A, et al. Diagnostic performance of quantitative kappa and lambda free light chain assays in clinical practice. *Clin Chem* 2005 May;51(5):878-81.  
*Not relevant re test, population, diagnosis, or comparison.*
94. Katzmman JA. Serum free light chain specificity and sensitivity: a reality check. *Clin Chem* 2006 Sep;52(9):1638-39.  
*Narrative review or commentary.*
95. Katzmman JA, Stankowski-Drengler TJ, Kyle RA, et al. Specificity of serum and urine protein electrophoresis for the diagnosis of monoclonal gammopathies. *Clin Chem* 2010 Dec;56(12):1899-900.  
*Not relevant re test, population, diagnosis, or comparison.*
96. Keren DF. Heavy/Light-chain analysis of monoclonal gammopathies. *Clin Chem* 2009 Sep;55(9):1606-08.  
*Not relevant re test, population, diagnosis, or comparison.*
97. Khalifa MB, Weidenhaupt M, Choulier L, et al. Effects on interaction kinetics of mutations at the VH-VL interface of Fabs depend on the structural context. *Journal of Molecular Recognition* 2000 May;13(3):127-39.  
*Not relevant re test, population, diagnosis, or comparison.*

98. Kim Y, Wall JS, Meyer J, et al. Thermodynamic modulation of light chain amyloid fibril formation. *Journal of Biological Chemistry* 2000 Jan 21;275(3):1570-74.  
*Not relevant re test, population, diagnosis, or comparison.*
99. Kleeberg L, Morgera S, Jakob C, et al. Novel renal replacement strategies for the elimination of serum free light chains in patients with kappa light chain nephropathy. *European Journal of Medical Research* 2009 Feb 18;14(2):47-54.  
*Not relevant re test, population, diagnosis, or comparison.*
100. Klein CJ, Vrana JA, Theis JD, et al. Mass spectrometric-based proteomic analysis of amyloid neuropathy type in nerve tissue. *Archives of Neurology* 2011 Feb;68(2):195-99.  
*Not relevant re test, population, diagnosis, or comparison.*
101. Kuci H, Ebert MP, Rocken C. Anti-lambda-light chain-peptide antibodies are suitable for the immunohistochemical classification of AL amyloid. *Histology & Histopathology* 2007 Apr;22(4):379-87.  
*Not relevant re test, population, diagnosis, or comparison.*
102. Kumar S, Dispenzieri A, Gertz MA. High-dose melphalan versus melphalan plus dexamethasone for AL amyloidosis. *New England Journal of Medicine* 2008 Jan 3;358(1):91-93.  
*Letter without data.*
103. Kyle RA, Gertz MA, Witzig TE, et al. Review of 1027 patients with newly diagnosed multiple myeloma. *Mayo Clinic Proceedings* 2003 Jan;78(1):21-33.  
*Not relevant re test, population, diagnosis, or comparison.*
104. Kyle RA. New strategies for MGUS and smoldering multiple myeloma. *Clinical Advances in Hematology & Oncology* 2004;2(8):507.  
*Not relevant re test, population, diagnosis, or comparison.*
105. Kyle RA, Rajkumar SV. Monoclonal gammopathy of undetermined significance. [Review] [103 refs]. *Clinical Lymphoma & Myeloma* 2005 Sep;6(2):102-14.  
*Narrative review or commentary.*
106. Kyle RA, Rajkumar SV. Monoclonal gammopathy of undetermined significance and smoldering multiple myeloma: emphasis on risk factors for progression. [Review] [84 refs]. *British Journal of Haematology* 2007 Dec;139(5):730-43.  
*Narrative review or commentary.*
107. Lachmann HJ, Wechalekar AD, Gillmore JD. High-dose melphalan versus melphalan plus dexamethasone for AL amyloidosis. *New England Journal of Medicine* 2008;358(1):91-92.  
*Letter without data.*
108. Lae ME, Vencio EF, Inwards CY, et al. Myeloma of the jaw bones: a clinicopathologic study of 33 cases. *Head & Neck* 2003 May;25(5):373-81.  
*Not relevant re test, population, diagnosis, or comparison.*
109. Le BT, Bengoufa D, Benlakehal M, et al. Urinary free light chain analysis by the Freelite immunoassay: a preliminary study in multiple myeloma. *Clinical Biochemistry* 2002 Oct;35(7):565-67.  
*Not relevant re test, population, diagnosis, or comparison.*
110. Lee LN, Jan IS, Tien HF, et al. Laboratory and clinical characterization of monoclonal gammopathy in Taiwanese. *Journal of the Formosan Medical Association* 2002 Feb;101(2):91-97.  
*Not relevant re test, population, diagnosis, or comparison.*
111. Lee MS, Lee GM. Hyperosmotic pressure enhances immunoglobulin transcription rates and secretion rates of KR12H-2 transfectoma. *Biotechnology & Bioengineering* 2000 May 5;68(3):260-68.  
*Not relevant re test, population, diagnosis, or comparison.*
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## Appendix C: Quality Criteria and Individual Study Grades

Table for Key Question 1

Author Year [PMID]	Prospective/Retrospective	Selection/spectrum bias	Case-control design	Consecutive patient selection	Lack of verification bias	Blinded index-test readers	Proper analysis if repeated sampling	Time interval between index and reference test reported	Statistical test used to quantify uncertainty	Quality Grade	Summary of grade rationale
Abadie 2006 <sup>1</sup> [16682511]	R	Y	N	Y	Y	N	Y	N	N	B	No measure of statistical uncertainty, no major biases, clear description of population
Piehler 2008 <sup>2</sup> [18801937]	P	Y	N	Y	Y	N	Y	N	N	B	No measure of statistical uncertainty, no major biases, consecutive recruitment
Vermeersch 2008 <sup>3</sup> [18729849]	R	Y	Y	Y	Y	ND	Y	N	N	B	No measure of statistical uncertainty, described sample, no major biases

Y= Yes, N = No, ND = not described, P = Prospective study design, R = Retrospective study design.  
 Types of bias are defined in Glossary and also described at the end of each row under “Summary of grade rationale.”  
 Criteria are derived from STARD ([www.stard-statement.org](http://www.stard-statement.org)) and STROBE ([www.strobe-statement.org](http://www.strobe-statement.org)).

Table for Key Questions 4–5

Author Year [PMID]	Prospective/ Retrospective	Outcomes clearly defined	Bias present	Confounders clearly defined/ analyzed	Loss to follow up explained	Population clearly described	Data lost/not analyzed/ missing	Inclusion/ exclusion criteria defined	Quality grade	Summary of grade rationale
<b>Key Question 4</b>										
Dispenzieri, 2008 <sup>4</sup> [18364469]	R	Y	Y	N	ND	Y	N	Y	B	Retrospective without adjustment
Giarin, 2009 <sup>5</sup> [19520760]	R	Y	Y	N	ND	Y	N	Y	B	Retrospective without adjustment
Khoriaty, 2010 <sup>6</sup> [20223721]	R	Y	Y	N	ND	Y	N	Y	C	Small sample size, retrospective without adjustment
Kroger, 2010 <sup>7</sup> [2043663]	?	N	?	N	ND	N	N	Y	C	Letter to the editor with limited information, small sample size, SFLC response definitions not described, few details about study design, limited data
Kumar 2011 <sup>8</sup> [21328431]	R	Y	Y	N	ND	Y	N	Y	C	Retrospective, extreme selection/spectrum bias
Kyrtsonis, 2007 <sup>9</sup> [17408464]	P	Y	Y	N	ND	N	N	Y	C	Limited information about patient recruitment and study design, small sample size
Lachmann 2003 <sup>10</sup> [12823348]	P	Y	Y	N	ND	Y	N	Y	C	Retrospective, selection/spectrum bias, sample not uniformly treated
Sanchorawala 2005 <sup>11</sup> [16044137]	R	Y	N	N	ND	Y	N	Y	C	Retrospective, small sample size
Van Rhee, 2007 <sup>12</sup> [17416735]	P	Y	?	N	ND	Y	N	Y	B	Retrospective with adjustment
<b>Key Question 5</b>										
Chee 2009 <sup>13</sup> [19641191]	R	n	?	N	ND	N	N	Y	C	Small sample, selection/spectrum bias

Y= Yes, N = No, ND = not described, P = Prospective study design, R = Retrospective study design, ? = unclear.  
Types of bias are defined in Glossary and also described at the end of each row under “Summary of grade rationale.”  
Criteria are derived from STARD ([www.stard-statement.org](http://www.stard-statement.org)) and STROBE ([www.strobe-statement.org](http://www.strobe-statement.org)).

## Appendix C References

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