**Health-related quality of life and functional status of patients with chronic graft-versus-host disease: a systematic literature review**

**Manuscript supplement**

**SUPPLEMENTARY MATERIALS**

*Table S1. Literature search strategy*

| **Search** **number** | **Search area** | **PubMed** |
| --- | --- | --- |
| **Search termsa** | **Number of search hitsb** |
| #1 | Disease | ((chronic[Title/Abstract] AND ("graft versus host disease"[Title/Abstract] OR "graft-versus-host disease"[Title/Abstract] OR "graft vs host disease"[Title/Abstract] OR "graft-vs-host disease"[Title/Abstract] OR GVHD[Title/Abstract] OR "homologous wasting disease"[Title/Abstract])) OR cGVHD[Title/Abstract] OR c-GVHD[Title/Abstract] OR (overlap[Title/Abstract] AND ("graft versus host disease"[Title/Abstract] OR "graft-versus-host disease"[Title/Abstract] OR "graft vs host disease"[Title/Abstract] OR "graft-vs-host disease"[Title/Abstract] OR GVHD[Title/Abstract])))  | 8,542 |
| #2 | Epidemiology | (inciden\*[Title/Abstract] OR prevalen\*[Title/Abstract] OR frequen\*[Title/Abstract] OR epidemiolog\*[Title/Abstract] OR rate[Title/Abstract])  | 4,045,449 |
| #3 | Humanistic burden | ("quality of life" [Title/Abstract] OR utility [Title/Abstract] OR HRQol [Title/Abstract] OR QoL[Title/Abstract] OR "humanistic burden" [Title/Abstract] OR "quality adjusted life years" [Title/Abstract] OR "quality-adjusted life years"[Title/Abstract] OR QALY[Title/Abstract] OR "disability adjusted life year"[Title/Abstract] OR "disability-adjusted life year"[Title/Abstract] OR DALY[Title/Abstract])  | 358,860 |
| #4 | Economic burden | ((cost [Title/Abstract] AND burden[Title/Abstract] ) OR "burden of disease" [Title/Abstract] OR "burden of illness" [Title/Abstract] OR "economic burden" [Title/Abstract] OR "resource burden" [Title/Abstract] OR "financial burden" [Title/Abstract] OR "economic consequences" [Title/Abstract] OR "cost of illness" [Title/Abstract] OR "healthcare cost" [Title/Abstract] OR "cost of disease" [Title/Abstract] OR "cost analysis" [Title/Abstract] OR "cost assessment" [Title/Abstract] OR "cost study" [Title/Abstract] OR "resource use" [Title/Abstract] OR "healthcare resources" [Title/Abstract] OR "resource utilization" [Title/Abstract] OR expenditure[Title/Abstract] OR "out of pocket" [Title/Abstract] OR "patient cost" [Title/Abstract] OR "co-payment" [Title/Abstract] OR "private expenditure" [Title/Abstract] OR "patient time" [Title/Abstract] OR "carer cost" [Title/Abstract] OR "carer expenditure" [Title/Abstract] OR "carer time" [Title/Abstract] OR "caregiver cost" [Title/Abstract] OR "caregiver expenditure" [Title/Abstract] OR "caregiver time" [Title/Abstract] OR coinsurance [Title/Abstract] OR "co-pay" [Title/Abstract] OR "co payment" [Title/Abstract] OR "co-payment" [Title/Abstract] OR "patient's cost" [Title/Abstract] OR "patients' cost"[Title/Abstract] OR "societal cost" [Title/Abstract] OR "social cost" [Title/Abstract] OR "social care cost" [Title/Abstract] OR "work loss" [Title/Abstract] OR "work absenteeism" [Title/Abstract] OR "productivity loss" [Title/Abstract] OR "lost productivity" [Title/Abstract] OR "productivity impairment" [Title/Abstract] OR earnings [Title/Abstract] OR "educational attainment" [Title/Abstract] OR "educational achievement" [Title/Abstract] OR "educational impairment" [Title/Abstract] OR "occupational attainment" [Title/Abstract] OR "occupational achievement" [Title/Abstract] OR "occupational impairment" [Title/Abstract] OR "social functioning" [Title/Abstract] OR "social impairment" [Title/Abstract] OR "caregiver burden" [Title/Abstract] OR "carer burden" [Title/Abstract] OR "family burden" [Title/Abstract] OR "lost time" [Title/Abstract] OR "days absent" [Title/Abstract] OR "sick days" [Title/Abstract] OR "miss work" [Title/Abstract] OR "miss school" [Title/Abstract] OR "familial burden" [Title/Abstract] OR "family life" [Title/Abstract] OR "home responsibilities"[Title/Abstract])  | 115,781 |
| #5 | Combined searches | #1 AND #2 | 3,680 |
| #6 | #1 AND #3 | 317 |
| #7 | #1 AND #4 | 33 |
| #8 | #1 AND (#2 OR #3 OR #4) | 3,881 |
| #9 | Combined searches limited to papers written in English | #1 AND #2 Filters: English | 3,397 |
| #10 | #1 AND #3 Filters: English | 303 |
| #11 | #1 AND #4 Filters: English | 33 |
| #12 | #1 AND (#2 OR #3 OR #4) Filters: English | 3,591 |
| #13 | Combined searches limited to papers written in English and published 2007-2017 | #1 AND #2 Filters: Publication date from 2007/01/01 to 2017/12/31; English | 1,887 |
|  |  |  |
| #14 | #1 AND #3 Filters: Publication date from 2007/01/01 to 2017/12/31; English | 217 |
| #15 | #1 AND #4 Filters: Publication date from 2007/01/01 to 2017/12/31; English | 26 |
| #16 | #1 AND (#2 OR #3 OR #4) Filters: Publication date from 2007/01/01 to 2017/12/31; English | 2,026 |
| #17 | Combined searches limited to papers written in English, published 2007-2017, on human subjects | #1 AND #2 Filters: Publication date from 2007/01/01 to 2017/12/31; Humans; English | 1,575 |
| #18 | #1 AND #3 Filters: Publication date from 2007/01/01 to 2017/12/31; Humans; English | 170 |
| #19 | #1 AND #4 Filters: Publication date from 2007/01/01 to 2017/12/31; Humans; English | 20 |
| #20 | **#1 AND (#2 OR #3 OR #4) Filters: Publication date from 2007/01/01 to 2017/12/31; Humans; English** | **1,682** |

a: Search operators: AND is the operator for intersection; OR is the operator of union; [Title/Abstract] a combined field that searches Abstracts, and Titles; \* replaces multiple characters anywhere in a word

b: Literature search was conducted on May 30, 2017.

*Table S2. Results of the quality assessment*

|  |  |
| --- | --- |
| **First author, year** | **National of Institutes of Health Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies**  |
| **Q 1** | **Q 2** | **Q 3** | **Q 4** | **Q 5** | **Q 6** | **Q 7** | **Q 8** | **Q 9** | **Q 10** | **Q 11** | **Q 12** | **Q 13** | **Q 14** | **Quality rating** |
| Amin, 2015 [20] | Yes | Yes | No | No | No | NA | Yes | Yes | No | No | Yes | No | No | No | Good |
| Baird, 2013 [31] | Yes | Yes | Yes | Yes | No | No | No | Yes | Yes | No | Yes | NR | NA | No | Fair |
| Bassim, 2014 [32] | Yes | Yes | Yes | Yes | No | Yes | No | Yes | Yes | No | Yes | NR | NA | No | Fair |
| Bassim, 2015 [33] | Yes | Yes | Yes | Yes | No | No | No | Yes | Yes | No | No | NR | NA | No | Fair |
| DeLoss, 2016\* | Yes | Yes | No | No | No | NA | Yes | Yes | No | No | Yes | No | No | No | Poor |
| DePalo, 2015 [21] | Yes | Yes | Yes | Yes | No | No | NR | Yes | Yes | Yes | Yes | NR | NR | Yes | Good |
| El-Jawahri, 2014 [30] | Yes | Yes | Yes | Yes | No | NA | No | Yes | Yes | No | Yes | NR | NA | Yes | Good |
| Imanguli, 2010 [34] | Yes | Yes | Yes | Yes | No | Yes | No | Yes | Yes | No | Yes | NR | NA | No | Fair |
| Inamoto, 2012 [22] | Yes | Yes | Yes | Yes | No | NA | Yes | Yes | Yes | NA | Yes | NR | NR | Yes | Good |
| Inamoto, 2014 [23] | Yes | Yes | Yes | Yes | No | No | Yes | Yes | Yes | Yes | Yes | NR | NR | Yes | Good |
| Martines, 2011 [35] | Yes | Yes | Yes | Yes | No | No | No | Yes | Yes | No | Yes | NR | NA | No | Fair |
| Mo, 2013 [36] | Yes | Yes | Yes | Yes | No | Yes | No | Yes | Yes | No | Yes | NR | NA | Yes | Good |
| Pidala, 2011 [37] | Yes | Yes | Yes | Yes | No | Yes | No | Yes | Yes | No | Yes | NR | NA | Yes | Good |
| Pidala, 2011 [26] | Yes | Yes | Yes | Yes | No | Yes | NR | Yes | Yes | Yes | Yes | NR | NR | Yes | Good |
| Pidala, 2012 [27] | Yes | Yes | Yes | Yes | No | Yes | NR | Yes | Yes | No | Yes | NR | NR | No | Fair |
| Pidala, 2013 [24] | Yes | Yes | Yes | Yes | No | Yes | NR | Yes | Yes | Yes | Yes | NR | NR | Yes | Good |
| Pidala, 2013 [25] | Yes | Yes | Yes | Yes | No | Yes | NR | Yes | Yes | Yes | Yes | NR | NR | Yes | Good |
| Sun, 2015 [28] | Yes | Yes | Yes | Yes | No | No | NR | Yes | Yes | Yes | Yes | NR | NR | Yes | Good |
| Wong, 2010 [29] | Yes | Yes | No | Yes | No | No | Yes | Yes | Yes | Yes | Yes | NR | No | Yes | Good |

NA: not applicable; NR: not reported; Q: question

\*: DeLoss KS, Le H-G, Gire A, et al. PROSE treatment for ocular chronic graft-versus-host disease as a clinical network expands. Eye & Contact Lens. 2016;42:262-266. –excluded from the review because of poor quality

*Table S3. Health-reported quality of life data for patients with chronic graft-versus-host disease reported in the included studies*

|  |  |  |
| --- | --- | --- |
| **First author, year** | **HRQoL instrument** | **HRQoL data** |
| Amin, 2015 [20] | EORTC QLQ-C30 | Mean (95% CI)a, bPatients with no or mild cGVHD, no BOS: Global health at month 6 after transplantation 68 (65 - 71); Global health at year 2 after transplantation 72 (64 - 80) Patients with moderate or severe cGVHD, no BOS: Global health at month 6 after transplantation 64.5 (61 - 68); Global health at year 2 after transplantation 71 (60 - 82) Patients with moderate or severe cGVHD and BOS: Global health at month 6 after transplantation 70 (65.5 - 74.5); Global health at year 2 after transplantation 65.5 (56 - 75) |
| SF-36 | Mean (95% CI)a, b Patients with no or mild cGVHD, no BOS: PCS at month 6 after transplantation 41 (40 - 42); PCS at year 2 after transplantation 45 (42 - 48); MCS at month 6 after transplantation 52 (50.5 - 53.5); MCS at year 2 after transplantation 57 (53 - 61)Patients with moderate or severe cGVHD, no BOS: PCS at month 6 after transplantation 40 (38 - 42); PCS at year 2 after transplantation 40 (35 - 45); MCS at month 6 after transplantation 54 (52 - 56); MCS at year 2 after transplantation 60 (54.5 - 65.5)Patients with moderate or severe cGVHD and BOS: PCS at month 6 after transplantation 40 (38 - 42); PCS at year 2 after transplantation 39 (35 - 43); MCS at month 6 after transplantation 53.5 (51 - 56); MCS at year 2 after transplantation 57 (52 - 62) |
| SGRQ | Mean (95% CI)a, bPatients with no or mild cGVHD, no BOS: Total at month 6 after transplantation 14 (12 - 16); Total at year 2 after transplantation 12 (4 - 20)Patients with moderate or severe cGVHD, no BOS: Total at month 6 after transplantation 14 (10 - 18); Total at year 2 after transplantation 11 (0 - 22)Patients with moderate or severe cGVHD and BOS: Total at month 6 after transplantation 14 (10 - 18); Total at year 2 after transplantation 31.5 (21 - 42) |
| Baird, 2013 [31] | FACT-BMT | NR |
| SF-36 | NR |
| Bassim, 2014 [32] | FACT-BMT | NR |
| SF-36 | Mean (SE)Well-nourished patients: PCS 38.04 (0.86); MCS NRMalnourished patients: PCS 31.06 (1.56); MCS NR |
| Bassim, 2015 [33] | OHIP-14 | NR |
| DePalo, 2015 [21] | FACT-BMT | Mean (minimum, maximum)a Isolated oral cGVHD: FACT-BMT total 110 (49, 138)Oral and extra-oral cGVHD: FACT-BMT total 107 (39, 147)Extra-oral cGVHD: FACT-BMT total 107 (62, 140) |
| SF-36 | Mean (minimum, maximum)a Isolated oral cGVHD: PCS 41 (25, 59); MCS 49 (25, 66)Oral and extra-oral cGVHD: PCS 39 (15, 59); MCS 47 (15, 68)Extra-oral cGVHD: PCS 37 (15, 61); MCS 46 (18, 65) |
| El-Jawahri, 2014 [30] | FACT-BMT | MedianAge ≤ 40: FACT-BMT total 106Age 40-60: FACT-BMT total 102Age ≥ 60: FACT-BMT total 109 |
| SF-36 | NR |
| Imanguli, 2010 [34] | FACT-G | NR |
| OHIP-14 | NR |
| Inamoto, 2012 [22] | FACT-BMT | NR |
| SF-36 | NR |
| Inamoto, 2014 [23] | FACT-G | Median (interquartile range)Joint/fascia present: FACT-G total 76 (62–87)Joint/fascia absent: FACT-G total 81 (69–90.3) |
| SF-36 | Median (interquartile range)Joint/fascia present: PCS 37 (31.1–43.5); MCS 47 (38–55.2)Joint/fascia absent: PCS 40 (32.2-47.9); MCS 51 (40.8-55.9) |
| Mo, 2013 [36] | SF-36 | Mean (SD)Mild cGVHD: PCS 51.1 (7.9); MCS 54.6 (9.1)Moderate cGVHD: PCS 48.0 (8.2); MCS 52.6 (9.8)Severe cGVHD: PCS 36.2 (11.0); MCS 47.4 (10.4) |
| Pidala, 2011 [37] | FACT-BMT | Median (range)All cGVHD patients: TOI 65.0 (22.0-92.0); FACT-G total 81.0 (29.0-107.0); FACT-BMT total 109.0 (48.1-142.0)Mild cGVHD: TOI 70.0 (38.0-91.0); FACT-G total 84.5 (55.0-107.0); FACT-BMT total 114.0 (69.0-142.0)Moderate cGVHD: TOI 67.8 (22.0-92.0); FACT-G total 84.1 (29.0-104.0); FACT-BMT total 111.0 (49.0-140.0)Severe cGVHD: TOI 58.5 (25.0-89.9); FACT-G total 73.4 (37.0-105.0); FACT-BMT total 98.7 (48.1-136.0) |
| SF-36 | Median (range)All cGVHD patients: PCS 39.2 (15.9-59.4); MCS 51.0 (15.3-68.4)Mild cGVHD: PCS 43.2 (19.9-59.3); MCS 53.8 (28.5-61.4)Moderate cGVHD: PCS 40.2 (15.9-59.4); MCS 51.4 (17.0-68.4)Severe cGVHD: PCS 36.3 (19.3-56.7); MCS 48.1 (15.3-65.8) |
| Pidala, 2011 [26] | FACT-BMT | Mean (SD)TOI 67.0 (0.6); FACT-G total 81.0 (0.6); FACT-BMT total 109 (0.8)  |
| SF-36 | Mean (SD)PCS 40.6 (0.4); MCS 49.3 (0.4) |
| Pidala, 2012 [27] | FACT-BMT | Median (range)Overlap GVHD: TOI, 64.7 (22-94); FACT-G total 79 (29-108); FACT-BMT total 106 (49-146)Classic cGVHD: TOI 65.7 (25-93); FACT-G total 81.5 (23-101); FACT-BMT total 108 (36-138) |
| SF-36 | Median (range)Overlap GVHD: PCS 39.3 (15.5-59.4); MCS 49.8 (15.3-65.8) Classic cGVHD: PCS 40.1 (16.6-60.7); MCS 53.0 (25-68.4) |
| Pidala, 2013 [24] | FACT-BMT | Median (minimum, maximum)TOI 64.0 (22.0, 95.0); FACT-G total 80.0 (23.0, 108); FACT-BMT total 106 (36.0, 146) |
| SF-36 | Median (minimum, maximum)PCS 39.2 (15.3, 60.7); MCS 49.8 (15.3, 68.4) |
| Pidala, 2013 [25] | FACT-BMT | NR |
| SF-36 | NR |
| Sun, 2015 [28] | FACT-BMT | NR |
| SF-36 | NR |
| Wong, 2010 [29] | COH-QOL-HCT | NR |

BOS: bronchiolitis obliterans syndrome; cGVHD: chronic graft-versus-host disease; CI: confidence interval; COH-QOL-HCT: City of Hope Quality of Life in Hematopoietic Cell Transplant; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30; FACT-BMT: Functional Assessment of Cancer Therapy - Bone Marrow Transplant; FACT-G: Functional Assessment of Cancer Therapy - General; GVHD: graft-versus-host disease; HRQoL: health-related quality of life; MCS: mental component score; NIH: National Institutes of Health; NR: not reported; OHIP-14: Oral Health Impact Profile 14; PCS: physical component score; SD: standard deviation; SF-36: Short Form Instrument 36; SGRQ: St. George's Respiratory Questionnaire; TOI: Trial Outcome Index

*Table S4. Functional capacity data for patients with chronic graft-versus-host disease reported in the included studies*

|  |  |  |
| --- | --- | --- |
| **First author, year** | **Functional capacity measure** | **Functional capacity data** |
| Baird, 2013 31 | HAP | NR |
| HGS | NR |
| 2-MWT | NR |
| Bassim, 2014 32 | HAP | Mean (SE)Well-nourished patients: HAP MAS 73.93 (1.09); HAP AAS 63.08 (1.40)Malnourished patients: HAP MAS 63.24 (2.29); HAP AAS 49.69 (2.86) |
| El-Jawahri, 2014 30 | HAP | NR |
| 2-MWT | MedianaAge ≤ 40: 504 feetAge 40-60: 501 feetAge ≥ 60: 454 feet |
| Inamoto, 2012 22 | HAP | NR |
| Inamoto, 2014 23 | HAP | Median (interquartile range)Joint/fascia present: HAP MAS 73 (61-82); HAP AAS 63 (51-74)Joint/fascia absent: HAP MAS 73 (62-82); HAP AAS 62 (48-73) |
| HGS | Median (interquartile range)Joint/fascia present: 55.8 (40-81.7) poundsJoint/fascia absent: 61 (42.3-79.7) pounds |
| 2-MWT | Median (interquartile range)Joint/fascia present: 482 (415-568) feetJoint/fascia absent: 500 (404-575) feet |
| Martires, 2011 35 | HGS | Mean (SE)Non-sclerotic cGVHD: 73.41 (3.03) poundsSclerotic cGVHD: 56.77 (2.10) pounds |
| 2-MWT | NR |
| Pidala, 2012 27 | HAP | Median (range)Overlap GVHD: HAP MAS 70 (36-94); HAP AAS 59 (14-94)Classic cGVHD: HAP MAS 78 (52-94); HAP AAS 70 (30-94) |
| HGS | Median (range)Overlap GVHD: 59.7 (2.0-167.0) poundsClassic cGVHD: 63.3 (15.3-139.0) pounds |
| 2-MWT | Median (range)Overlap GVHD: 495 (170-1150) feetClassic cGVHD: 540 (300-1140) feet |
| Pidala, 2013 24 | HAP | Median (minimum, maximum)HAP MAS 73.0 (36.0-94.0); HAP AAS 62.0 (14.0-94.0) |
| HGS | Median (minimum, maximum)59.9 (2.0-167) pounds |
| 2-MWT | Median (minimum, maximum)500 (170-1150) feet |
| Pidala, 2013 25 | HAP | NR |
| HGS | Median (minimum, maximum)60 (2-167) pounds |
| 2-MWT | Median (minimum, maximum)500 (170-1150) feet |
| Sun, 2015 28 | HAP | NR |

2-MWT: 2-minute walk test; AAS: adjusted activity score; cGVHD: chronic graft-versus-host disease; GVHD: graft-versus-host disease; HAP: Human Activity Profile; HGS: hand grip strength; MAS: maximum activity score; SE: standard error