



# 医学雑誌業界変遷の傾向と対策

## - 医学論文投稿のお作法を知る -

国立がん研究センター中央病院  
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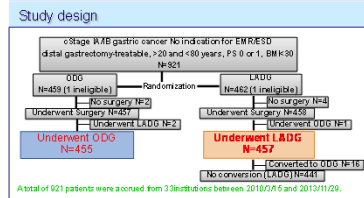
片山 宏

2017年10月14日 第20回JCOG臨床試験セミナー（中級編）

# はじめに

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| <b>Background</b> <ul style="list-style-type: none"> <li>The safety of laparoscopy-assisted distal gastrectomy (LADG) with nodal dissection for stage IA and IB gastric cancer has been already reported in our previous phase I study.<sup>1</sup></li> <li>Although the number of patients undergoing LADG has been increasing, there is no confirmatory randomized controlled trial (RCT) to evaluate the efficacy of LADG compared with open distal gastrectomy (ODG).</li> </ul> |                                                                                                                                                                                                                                                            |
| <b>Objectives</b> <ul style="list-style-type: none"> <li>We conducted a RCT to confirm the non-inferiority of overall survival (OS) of LADG to ODG in patients with clinical IA (T1N0) or IB (T1N1 or T2/M0) gastric cancer.</li> <li>Safety and short-term outcome are presented.</li> </ul>                                                                                                                                                                                         |                                                                                                                                                                                                                                                            |
| <b>Endpoints &amp; Statistical Methods</b>                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                            |
| <b>Primary endpoint</b> <ul style="list-style-type: none"> <li>Overall survival (OS)</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                       | We anticipate 5 years of follow-up after 5 years of accrual, ensuring at least 80% power with a one-sided alpha of 5% and a non-inferiority margin of 5% in terms of 5-year survival. This assumes an expected 5-year overall survival of 90% in each arm. |
| <b>Secondary endpoint</b> <ul style="list-style-type: none"> <li>Relapse-free survival (RFS)</li> <li>Proportion of conversion to open surgery</li> <li>Adverse events</li> <li>Short-term clinical outcomes</li> <li>Postoperative quality of life (QOL)</li> </ul>                                                                                                                                                                                                                  | <b>Planned accrual: 5 years</b><br><b>Actual accrual:</b> 15/02/2010–29/11/2013<br><b>Latest analysis:</b> 16/12/2014                                                                                                                                      |
| <b>Sample size: 920</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                            |



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| <b>Key eligibility criteria</b> <ol style="list-style-type: none"> <li>1) Histologically proven gastric adenocarcinoma.</li> <li>2) Clinical stage IA (T1N0) or IB (T1N1, T2/M0) according to the Japanese Classification of Gastric Carcinoma, Second English edition<sup>2</sup>.</li> <li>3) In case without preceding endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD), either "cT1" or "cN0" and no indication of EMR is eligible.</li> <li>4) In case with preceding EMR or ESD, the following conditions are fulfilled:                         <ol style="list-style-type: none"> <li>(i) pathological findings require additional gastrectomy,</li> <li>(ii) within 91 days from EMR, (iii) no perforation by EMR, (iv) resection margin of EMR did not reach to the upper third of the stomach</li> </ol> </li> <li>5) Tumor located in the middle or lower third of the stomach, and curative resection is expected to be achievable by distal gastrectomy.</li> <li>6) Aged 20–80 years.</li> <li>7) PS (ECOG) of 0 or 1.</li> <li>8) A body mass index of 30.</li> <li>9) No prior treatment of chemotherapy or radiation therapy against any other malignancies.</li> </ol> |  |
| <b>Eligibility criteria of the surgeons and quality control</b> <ul style="list-style-type: none"> <li>Only the surgeons credentialized by the study chair can be responsible for both LADG and ODG.</li> <li>In the ODG arm, the experience of 60 or more open gastrectomies is needed.</li> <li>In the LADG arm, the experience of 30 or more LADGs and the certification or its equivalent by the Japan Society for Endoscopic Surgery are needed.</li> <li>All the LADG procedures are centrally reviewed by Endoscopists.</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |  |
| <b>Operative procedures</b> <ul style="list-style-type: none"> <li>The extent of nodal dissection is decided according to the surgical T and N stage which is based on the third version of the Gastric Cancer Treatment Guideline in Japan<sup>3</sup>.</li> <li>D1 or more dissection is applied for clinical stage IA tumor.</li> <li>D2 dissection is applied for clinical stage IB tumor.</li> <li>For clinical T1 gastric cancer having 4 cm or more margin from the pylorus, pylorus-preserving distal gastrectomy is allowed.</li> <li>Bursotomy is not allowed but preservation of omentum and/or vagus nerve is discretionary.</li> <li>In the LADG arm, &gt;5 cm of the mini-laparotomy incision is not allowed.</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |  |

If the intraoperative findings reveal a tumor stage of II or greater, the LADG is converted to an open surgery. <sup>1) Japanese Gastric Cancer Association, Japanese Classification of Gastric Carcinoma, Vol. 1, 2nd English Edition, Gastric Cancer 1999;10:24</sup>

|                                        |                            |
|----------------------------------------|----------------------------|
| <b>Patient characteristics (n=921)</b> |                            |
| Age, Median (Range)                    | ODG (n=455)<br>64 (27–80)  |
| Gender                                 | LADG (n=467)<br>63 (25–80) |
| Male / Female                          | 275 / 184                  |
| Clinical T stage                       | 411 / 48                   |
| T1 / T2                                | 411 / 48                   |
| Unknown                                | 0                          |
| Clinical N stage                       | 450 / 9                    |
| N0 / N1                                | 450 / 9                    |
| Unknown                                | 0                          |
| Clinical stage                         | 402 / 57                   |
| cIA / cIB                              | 401 / 60                   |
| Unknown                                | 1                          |
| PS                                     | 0 / 1                      |
| Preoperative BMI                       | 458 / 1                    |
| Median (Range)                         | 22.6 (16.2–29.7)           |
|                                        | 22.3 (15.2–28.5)           |

|                                                 |                               |
|-------------------------------------------------|-------------------------------|
| <b>Operative details (n=912)</b>                |                               |
| Operating time (minutes), Median (Range)        | ODG (n=455)<br>194 (48–446)   |
|                                                 | LADG (n=457)<br>278 (120–577) |
|                                                 | P-value<br>p<0.001            |
| Blood loss (ml), Median (Range)                 | ODG (n=455)<br>115 (0–890)    |
|                                                 | LADG (n=457)<br>38 (0–1900)   |
|                                                 | P-value<br>p<0.001            |
| Number of lymph nodes retrieved, Median (Range) | ODG (n=455)<br>39 (11–114)    |
|                                                 | LADG (n=457)<br>39 (8–94)     |
|                                                 | P-value<br>p=0.36             |
| Converted to ODG, %                             | ODG (n=455)<br>0              |
|                                                 | LADG (n=457)<br>16 (3.6)      |
|                                                 | P-value<br>p=0.033            |
| Operative procedure (%)                         | ODG (n=455)<br>333 (73.0)     |
|                                                 | LADG (n=457)<br>342 (74.8)    |
|                                                 | P-value<br>p=0.85             |
| Distal gastrectomy                              | ODG (n=455)<br>122 (26.8)     |
|                                                 | LADG (n=457)<br>114 (24.8)    |
|                                                 | P-value<br>p=0.85             |
| Pylorus preserving gastrectomy                  | ODG (n=455)<br>0              |
|                                                 | LADG (n=457)<br>0             |
|                                                 | P-value<br>p=0.999            |

|                                                 |                                 |
|-------------------------------------------------|---------------------------------|
| <b>Short-term clinical outcomes (n=912)</b>     |                                 |
| Proportion of required analgesic on POD 0–10, % | ODG (n=455)<br>279 (59.3)       |
|                                                 | LADG (n=457)<br>230 (50.3)      |
|                                                 | P-value<br>p=0.006              |
| First fever, POD                                | ODG (n=455)<br>3 (0–12)         |
|                                                 | LADG (n=457)<br>2 (0–7)         |
|                                                 | P-value<br>p<0.0001             |
| First shiver, POD                               | ODG (n=455)<br>37.7 (0.2–39.3)  |
|                                                 | LADG (n=457)<br>37.8 (0.6–39.3) |
|                                                 | P-value<br>p=0.36               |
| The highest during in-hosp.                     | ODG (n=455)<br>37.8 (0.6–39.3)  |
|                                                 | LADG (n=457)<br>37.8 (0.6–39.3) |
|                                                 | P-value<br>p=0.36               |

|                                              |                    |
|----------------------------------------------|--------------------|
| <b>Intraoperative adverse events (n=912)</b> |                    |
| Thromboembolic event                         | ODG (n=455)<br>0   |
|                                              | LADG (n=457)<br>0  |
|                                              | P-value<br>p=0.999 |
| Intraoperative hepatobiliary injury          | ODG (n=455)<br>0   |
|                                              | LADG (n=457)<br>0  |
|                                              | P-value<br>p=0.999 |
| Intraoperative arterial injury               | ODG (n=455)<br>0   |
|                                              | LADG (n=457)<br>0  |
|                                              | P-value<br>p=0.999 |
| Intraoperative venous injury                 | ODG (n=455)<br>0   |
|                                              | LADG (n=457)<br>0  |
|                                              | P-value<br>p=0.999 |
| Intraoperative gastrointestinal injury       | ODG (n=455)<br>0   |
|                                              | LADG (n=457)<br>0  |
|                                              | P-value<br>p=0.999 |
| Intraoperative splenic injury                | ODG (n=455)<br>0   |
|                                              | LADG (n=457)<br>0  |
|                                              | P-value<br>p=0.999 |

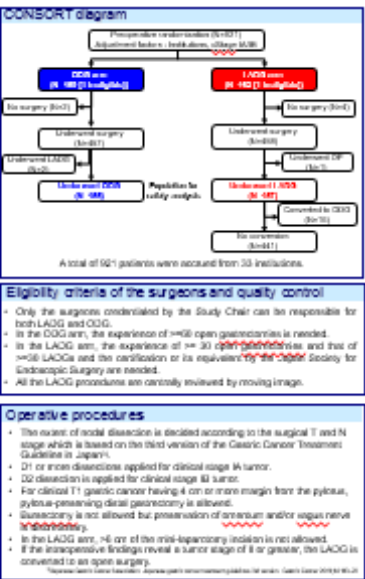
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|-------------------------------------------------------------|---------------------------|
| <b>In-hospital, non-hematological adverse event (n=912)</b> |                           |
| CTCAE v4.0 G3–4                                             | ODG (n=455)<br>21 (4.6%)  |
|                                                             | LADG (n=457)<br>19 (4.1%) |
|                                                             | P-value<br>p=0.85         |
| Overall                                                     | ODG (n=455)<br>21 (4.6%)  |
|                                                             | LADG (n=457)<br>19 (4.1%) |
|                                                             | P-value<br>p=0.85         |
| pancreatic fistula                                          | ODG (n=455)<br>2 (0.4%)   |
|                                                             | LADG (n=457)<br>2 (0.4%)  |
|                                                             | P-value<br>p=0.999        |
| Postoperative hemorrhage                                    | ODG (n=455)<br>0          |
|                                                             | LADG (n=457)<br>2 (0.4%)  |
|                                                             | P-value<br>p=0.999        |
| Intra-abdominal abscess                                     | ODG (n=455)<br>8 (1.8%)   |
|                                                             | LADG (n=457)<br>7 (1.5%)  |
|                                                             | P-value<br>p=0.85         |
| Anastomotic leak                                            | ODG (n=455)<br>1 (0.2%)   |
|                                                             | LADG (n=457)<br>1 (0.2%)  |
|                                                             | P-value<br>p=0.999        |
| Anastomotic stenosis                                        | ODG (n=455)<br>0          |
|                                                             | LADG (n=457)<br>0         |
|                                                             | P-value<br>p=0.999        |
| Cholecystitis                                               | ODG (n=455)<br>0          |
|                                                             | LADG (n=457)<br>0         |
|                                                             | P-value<br>p=0.999        |
| Dumping syndrome                                            | ODG (n=455)<br>0          |
|                                                             | LADG (n=457)<br>0         |
|                                                             | P-value<br>p=0.999        |
| Delay of gastric emptying                                   | ODG (n=455)<br>4 (0.9%)   |
|                                                             | LADG (n=457)<br>3 (0.7%)  |
|                                                             | P-value<br>p=0.85         |
| Gastro-esophageal regurgitation                             | ODG (n=455)<br>0          |
|                                                             | LADG (n=457)<br>0         |
|                                                             | P-value<br>p=0.999        |
| Obstructive ileus                                           | ODG (n=455)<br>1 (0.2%)   |
|                                                             | LADG (n=457)<br>1 (0.2%)  |
|                                                             | P-value<br>p=0.999        |
| Paralytic ileus                                             | ODG (n=455)<br>0          |
|                                                             | LADG (n=457)<br>0         |
|                                                             | P-value<br>p=0.999        |
| Thromboembolic event                                        | ODG (n=455)<br>0          |
|                                                             | LADG (n=457)<br>0         |
|                                                             | P-value<br>p=0.999        |
| Pneumonia                                                   | ODG (n=455)<br>4 (0.9%)   |
|                                                             | LADG (n=457)<br>1 (0.2%)  |
|                                                             | P-value<br>p=0.85         |
| Chyle leakage                                               | ODG (n=455)<br>0          |
|                                                             | LADG (n=457)<br>0         |
|                                                             | P-value<br>p=0.999        |
| Wound infection                                             | ODG (n=455)<br>0          |
|                                                             | LADG (n=457)<br>2 (0.4%)  |
|                                                             | P-value<br>p=0.999        |
| Wound dehiscence                                            | ODG (n=455)<br>1 (0.2%)   |
|                                                             | LADG (n=457)<br>0         |
|                                                             | P-value<br>p=0.999        |

|                                                                   |                            |
|-------------------------------------------------------------------|----------------------------|
| <b>Hematological and non-hematological adverse events (n=912)</b> |                            |
| CTCAE v4.0 G3–4                                                   | ODG (n=455)<br>1 (0.2%)    |
|                                                                   | LADG (n=457)<br>0          |
|                                                                   | P-value<br>p=0.999         |
| Overall                                                           | ODG (n=455)<br>1 (0.2%)    |
|                                                                   | LADG (n=457)<br>0          |
|                                                                   | P-value<br>p=0.999         |
| Leucopenia                                                        | ODG (n=455)<br>5 (1.1%)    |
|                                                                   | LADG (n=457)<br>6 (1.3%)   |
|                                                                   | P-value<br>p=0.85          |
| Anemia                                                            | ODG (n=455)<br>1 (0.2%)    |
|                                                                   | LADG (n=457)<br>1 (0.2%)   |
|                                                                   | P-value<br>p=0.999         |
| Thrombocytopenia                                                  | ODG (n=455)<br>1 (0.2%)    |
|                                                                   | LADG (n=457)<br>1 (0.2%)   |
|                                                                   | P-value<br>p=0.999         |
| Hypothrombinemia                                                  | ODG (n=455)<br>4 (0.9%)    |
|                                                                   | LADG (n=457)<br>2 (0.4%)   |
|                                                                   | P-value<br>p=0.85          |
| Elevation of AST                                                  | ODG (n=455)<br>19 (4.2%)   |
|                                                                   | LADG (n=457)<br>57 (12.5%) |
|                                                                   | P-value<br>p<0.001         |
| Elevation of ALT                                                  | ODG (n=455)<br>20 (4.4%)   |
|                                                                   | LADG (n=457)<br>54 (11.8%) |
|                                                                   | P-value<br>p<0.001         |
| Elevation of creatinine                                           | ODG (n=455)<br>1 (0.2%)    |
|                                                                   | LADG (n=457)<br>0          |
|                                                                   | P-value<br>p=0.999         |
| Hypertension                                                      | ODG (n=455)<br>5 (1.1%)    |
|                                                                   | LADG (n=457)<br>3 (0.7%)   |
|                                                                   | P-value<br>p=0.85          |
| Hypokalemia                                                       | ODG (n=455)<br>2 (0.4%)    |
|                                                                   | LADG (n=457)<br>0          |
|                                                                   | P-value<br>p=0.999         |
| Hypokarotemia                                                     | ODG (n=455)<br>2 (0.4%)    |
|                                                                   | LADG (n=457)<br>0          |
|                                                                   | P-value<br>p=0.999         |

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| <b>Conclusions</b>                                                                                                                                                                                                                                                                                           |  |
| Although the elevation of serum AST/ALT should be taken care, this trial confirmed that LADG performed by the credentialized surgeons was safe as ODG in terms of adverse event and short-term clinical outcomes.                                                                                            |  |
| LADG will be an alternative procedure in clinical IAB gastric cancer if the non-inferiority of LADG in OS is confirmed by the primary analysis planned in 2018.                                                                                                                                              |  |
| <b>Acknowledgement</b>                                                                                                                                                                                                                                                                                       |  |
| The study was supported in part by the National Cancer Center Research and Development Fund (26-4-1), the Grant-in-Aid for Clinical Cancer Research (24-01-01) and a Health Science Research Grant for Medical Frontier Strategy Research (16-003) from the Ministry of Health, Labour and Welfare of Japan. |  |

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| <b>Background</b> <ul style="list-style-type: none"> <li>The safety of laparoscopy-assisted distal gastrectomy (LADG) with nodal dissection for stage IA and IB gastric cancer has been already reported in our previous phase I study.<sup>1</sup></li> <li>Although the number of patients undergoing LADG has been increasing, there is no confirmatory randomized controlled trial (RCT) to evaluate the efficacy of LADG compared with open distal gastrectomy (ODG).</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                            |
| <b>Objectives</b> <ul style="list-style-type: none"> <li>We conducted a RCT to confirm the non-inferiority of overall survival (OS) of LADG to ODG in patients with clinical IA (T1N0) or IB (T1N1 or T2/M0) gastric cancer. Safety and short-term outcome are presented here.</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                            |
| <b>Key eligibility criteria</b> <ol style="list-style-type: none"> <li>1. Histologically proven gastric adenocarcinoma.</li> <li>2. Clinical stage IA (T1N0) or IB (T1N1, T2/M0) according to the Japanese Classification of Gastric Carcinoma, 2nd English edition<sup>2</sup>.</li> <li>3. In case without preceding endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD), either "cT1" or "cN0" and no indication of EMR is eligible.</li> <li>4. In case with preceding EMR or ESD, the following conditions are fulfilled:                         <ol style="list-style-type: none"> <li>(i) pathological findings require additional gastrectomy</li> <li>(ii) within 91 days from EMR (ESD)</li> <li>(iii) no perforation by EMR (ESD)</li> <li>(iv) resection margin of EMR (ESD) did not reach to the upper third of the stomach</li> </ol> </li> <li>5. Tumor located in the middle or lower third of the stomach, and curative resection is expected to be achievable by distal gastrectomy.</li> <li>6. Aged 20–80 years.</li> <li>7. PS (ECOG) of 0 or 1.</li> <li>8. A body mass index of 30 or less.</li> <li>9. No prior treatment of chemotherapy or radiation therapy against any other malignancies.</li> </ol> |                                                                                                                                                                                                                                                            |
| <b>Endpoints &amp; Statistical methods</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                                                                                                                                                                                                                            |
| <b>Primary endpoint</b> <ul style="list-style-type: none"> <li>Overall survival (OS)</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | We anticipate 5 years of follow-up after 5 years of accrual, ensuring at least 80% power with a one-sided alpha of 5% and a non-inferiority margin of 5% in terms of 5-year survival. This assumes an expected 5-year overall survival of 90% in each arm. |
| <b>Secondary endpoint</b> <ul style="list-style-type: none"> <li>Relapse-free survival (RFS)</li> <li>Proportion of conversion to open surgery</li> <li>Adverse events</li> <li>Short-term clinical outcomes</li> <li>Postoperative quality of life (QOL)</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | <b>Planned accrual: 5 years</b><br><b>Actual accrual:</b> 15/02/2010–29/11/2013<br><b>Latest analysis:</b> 16/12/2014                                                                                                                                      |
| <b>Sample size: 920</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                            |



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|----------------------------------------|----------------------------|
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| Age, Median (Range)                    | ODG (n=455)<br>64 (27–80)  |
| Gender                                 | LADG (n=467)<br>63 (25–80) |
| Male / Female                          | 275 / 184                  |
| Clinical T stage                       | 411 / 48                   |
| T1 / T2 / Unknown                      | 411 / 48 / 1               |
| Clinical N stage                       | 450 / 9                    |
| N0 / N1 / Unknown                      | 450 / 9 / 1                |
| Clinical stage                         | 402 / 57                   |
| cIA / cIB / Unknown                    | 401 / 60 / 1               |
| PS                                     | 0 / 1                      |
| Preoperative BMI                       | 458 / 1                    |
| Median (Range)                         | 22.6 (16.2–29.7)           |
|                                        | 22.3 (15.2–28.5)           |

|                                                 |                               |
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| <b>Operative details (n=912)</b>                |                               |
| Operating time (minutes), Median (Range)        | ODG (n=455)<br>194 (48–446)   |
|                                                 | LADG (n=457)<br>278 (120–577) |
|                                                 | P-value<br>p<0.001            |
| Blood loss (ml), Median (Range)                 | ODG (n=455)<br>115 (0–890)    |
|                                                 | LADG (n=457)<br>38 (0–1900)   |
|                                                 | P-value<br>p<0.001            |
| Number of lymph nodes retrieved, Median (Range) | ODG (n=455)<br>39 (11–114)    |
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|                                                 | P-value<br>p=0.36             |
| Operative procedure (%)                         | ODG (n=455)<br>333 (73.0%)    |
|                                                 | LADG (n=457)<br>342 (74.8%)   |
|                                                 | P-value<br>p=0.85             |
| Distal gastrectomy                              | ODG (n=455)<br>122 (26.8%)    |
|                                                 | LADG (n=457)<br>114 (24.8%)   |
|                                                 | P-value<br>p=0.85             |
| Pylorus preserving gastrectomy                  | ODG (n=455)<br>0              |
|                                                 | LADG (n=457)<br>0             |
|                                                 | P-value<br>p=0.999            |

|                                                   |                                 |
|---------------------------------------------------|---------------------------------|
| <b>Short-term clinical outcomes (n=912)</b>       |                                 |
| Proportion of required analgesic on POD 0–10, (%) | ODG (n=455)<br>279 (59.3%)      |
|                                                   | LADG (n=457)<br>230 (50.3%)     |
|                                                   | P-value<br>p=0.006              |
| First fever, POD                                  | ODG (n=455)<br>3 (0–12)         |
|                                                   | LADG (n=457)<br>2 (0–7)         |
|                                                   | P-value<br>p<0.001              |
| First shiver, POD                                 | ODG (n=455)<br>37.7 (0.2–39.3)  |
|                                                   | LADG (n=457)<br>37.8 (0.6–39.3) |
|                                                   | P-value<br>p=0.36               |
| The highest during in-hosp.                       | ODG (n=455)<br>37.8 (0.6–39.3)  |
|                                                   | LADG (n=457)<br>37.8 (0.6–39.3) |
|                                                   | P-value<br>p=0.36               |

|                                              |                    |
|----------------------------------------------|--------------------|
| <b>Intraoperative adverse events (n=912)</b> |                    |
| Thromboembolic event                         | ODG (n=455)<br>0   |
|                                              | LADG (n=457)<br>0  |
|                                              | P-value<br>p=0.999 |
| Intraoperative hepatobiliary injury          | ODG (n=455)<br>0   |
|                                              | LADG (n=457)<br>0  |
|                                              | P-value<br>p=0.999 |
| Intraoperative arterial injury               | ODG (n=455)<br>0   |
|                                              | LADG (n=457)<br>0  |
|                                              | P-value<br>p=0.999 |
| Intraoperative venous injury                 | ODG (n=455)<br>0   |
|                                              | LADG (n=457)<br>0  |
|                                              | P-value<br>p=0.999 |
| Intraoperative gastrointestinal injury       | ODG (n=455)<br>0   |
|                                              | LADG (n=457)<br>0  |
|                                              | P-value<br>p=0.999 |
| Intraoperative splenic injury                | ODG (n=455)<br>0   |
|                                              | LADG (n=457)<br>0  |
|                                              | P-value<br>p=0.999 |

|                                                   |                           |
|---------------------------------------------------|---------------------------|
| <b>In-hospital, non-hematological AEs (n=912)</b> |                           |
| CTCAE v4.0 G3–4                                   | ODG (n=455)<br>21 (4.6%)  |
|                                                   | LADG (n=457)<br>19 (4.1%) |
|                                                   | P-value<br>p=0.85         |
| Overall                                           | ODG (n=455)<br>21 (4.6%)  |
|                                                   | LADG (n=457)<br>19 (4.1%) |
|                                                   | P-value<br>p=0.85         |
| pancreatic fistula                                | ODG (n=455)<br>2 (0.4%)   |
|                                                   | LADG (n=457)<br>2 (0.4%)  |
|                                                   | P-value<br>p=0.999        |
| Postoperative hemorrhage                          | ODG (n=455)<br>0          |
|                                                   | LADG (n=457)<br>2 (0.4%)  |
|                                                   | P-value<br>p=0.999        |
| Intra-abdominal abscess                           | ODG (n=455)<br>8 (1.8%)   |
|                                                   | LADG (n=457)<br>7 (1.5%)  |
|                                                   | P-value<br>p=0.85         |
| Anastomotic leak                                  | ODG (n=455)<br>1 (0.2%)   |
|                                                   | LADG (n=457)<br>1 (0.2%)  |
|                                                   | P-value<br>p=0.999        |
| Anastomotic stenosis                              | ODG (n=455)<br>0          |
|                                                   | LADG (n=457)<br>0         |
|                                                   | P-value<br>p=0.999        |
| Cholecystitis                                     | ODG (n=455)<br>0          |
|                                                   | LADG (n=457)<br>0         |
|                                                   | P-value<br>p=0.999        |
| Dumping syndrome                                  | ODG (n=455)<br>0          |
|                                                   | LADG (n=457)<br>0         |
|                                                   | P-value<br>p=0.999        |
| Delay of gastric emptying                         | ODG (n=455)<br>4 (0.9%)   |
|                                                   | LADG (n=457)<br>3 (0.7%)  |
|                                                   | P-value<br>p=0.85         |
| Gastro-esophageal regurgitation                   | ODG (n=455)<br>0          |
|                                                   | LADG (n=457)<br>0         |
|                                                   | P-value<br>p=0.999        |
| Obstructive ileus                                 | ODG (n=455)<br>1 (0.2%)   |
|                                                   | LADG (n=457)<br>1 (0.2%)  |
|                                                   | P-value<br>p=0.999        |
| Paralytic ileus                                   | ODG (n=455)<br>0          |
|                                                   | LADG (n=457)<br>0         |
|                                                   | P-value<br>p=0.999        |
| Thromboembolic event                              | ODG (n=455)<br>0          |
|                                                   | LADG (n=457)<br>0         |
|                                                   | P-value<br>p=0.999        |
| Pneumonia                                         | ODG (n=                   |

# 本日の内容

- JCOG試験の論文がpublishされるまでの道のり
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- 論文投稿の際に知っておくべき各種ガイドライン
  - ICMJE recommendations / GPP guideline
  - CONSORT etc.

ICMJE: International Committee of Medical Journal Editors

GPP: Good Publication Practice

CONSORT: Consolidated Standards of Reporting Trials

# JCOG試験の結果公表の流れ

- 学会発表
  - 研究事務局による抄録の初稿作成
    - 抄録締切までの必要期間：解析後約1か月
  - 抄録レビューの流れ
    - 研究事務局→研究代表者・グループ代表委員（1名以上）  
→ **JCOG Data Center (DC)** → 研究事務局 → （英文校正） → 共同演者
  - 発表スライド（ポスター）レビューの流れ
    - 同上

本日の  
メインピック

- 論文公表
  - 研究事務局による初稿作成
    - 学会発表後1年以内に**DC**へ初稿を送付
  - 初稿レビューの流れ
    - 同上
  - Revise対応～accept～proof check
    - 主に研究事務局と**DC**で対応

# なぜDCレビュー？

- ヘルシンキ宣言（2013和文 No.36）

<http://dl.med.or.jp/dl-med/wma/helsinki2013j.pdf>

- すべての研究者、著者、編集者、発行者は研究結果の刊行と普及に倫理的責務がある
- 研究者は結果の公表の義務と、報告書の完全性と正確性の説明責任がある

- JCOGポリシー「結果の公表」

[http://www.jcog.jp/basic/policy/A\\_020\\_0010\\_26.pdf](http://www.jcog.jp/basic/policy/A_020_0010_26.pdf)

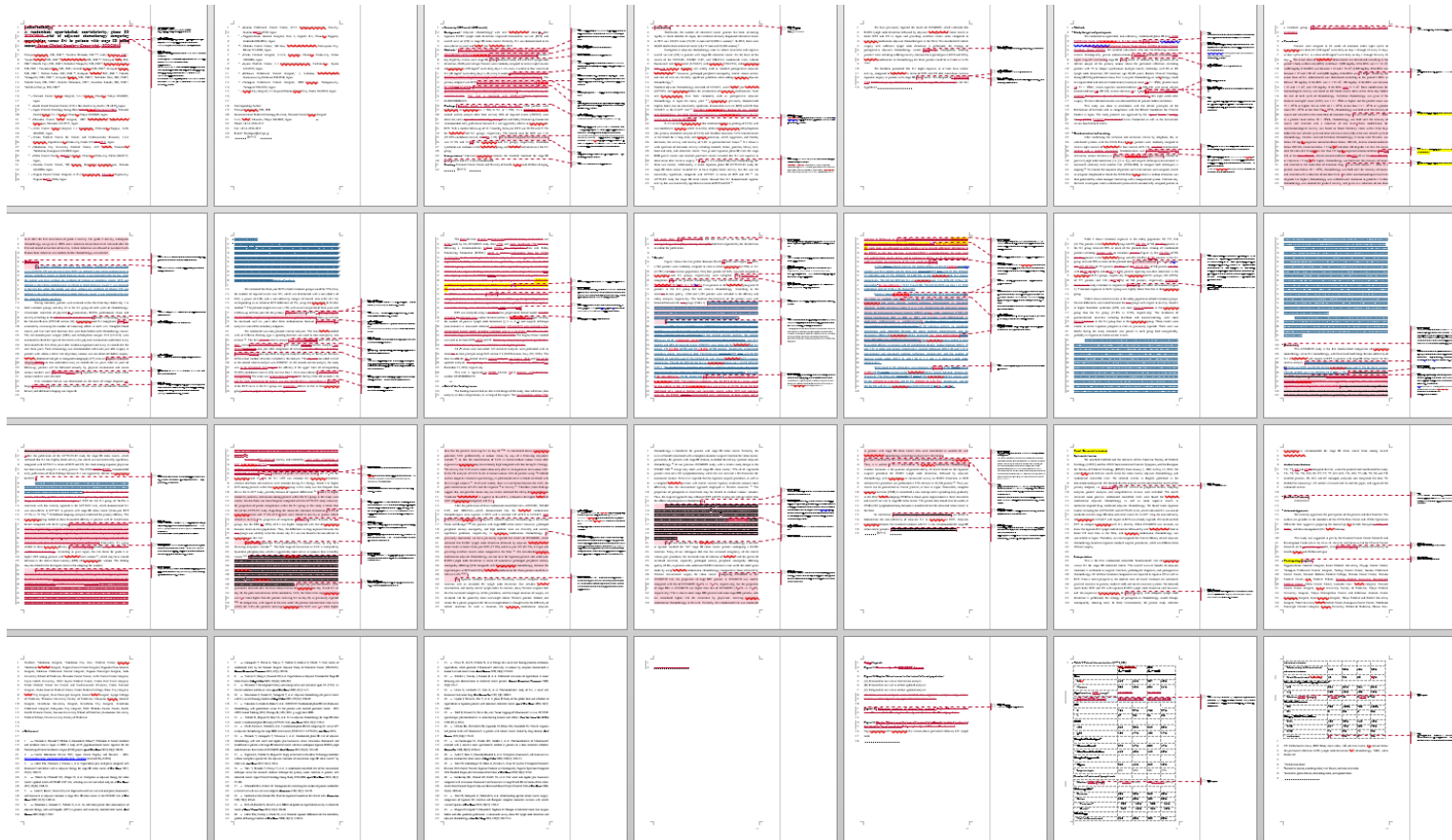
- 解析の責任者として統計担当は必ず共著者に含まれる
- 共著者の責務としてレビューを行う

# DC reviewの体制

- 全JCOG試験の発表をreview
  - 学会発表：25-35件/年, 論文：10-15件/年
- グループ担当者（MD2-3人, Stat, DM）+ DC長によるreview
  - 統計的事項の記載
  - 医学的事項の表現の適切さ
  - グループとしての結論・結果の解釈
  - マイクロエディット
- 共著者の場合、発表・論文全体への責任者としてDC reviewの取りまとめ役

研究（論文）の質をあげるための努力

# 論文reviewの例



- プロトコールとの整合性確認
- 数字の転記ミス修正
- 投稿雑誌に合わせた記載・体裁の変更

# DC reviewでよく指摘する事項

- データの転記ミスなしは稀（過去の100以上のJCOG試験論文のうち3論文のみ）
- 統計記載の章は大幅な書き換えをすることが多い
- 規定のword数を大幅に超過したabstractや本文（少しはOK）
- 冗長なintroduction
  - 背景記述、問題提示、活動記述、予測記述（仮説）の4部構成
- Tableとfigureの内容をresults本文にそのまま文章化
  - 情報の重複がないよう本文中には重要なものに限定
- Discussionの構成
  - 第1パラグラフにはresultsの要約を記載（resultsの繰り返しは×）
  - 得られた結果と既存の知識と比べた解釈
  - Limitation

参考資料 トム・ラングの医学論文「執筆・出版・発表」実践ガイド  
臨床研究と疫学研究のための国際ルール集（Part 2）

# 英語版プロトコール

- 臨床試験の場合、Major journal (NEJM、Lancet系、JCOなど)ではプロトコール提出が求められる
- Journalにより要求が異なる
  - NEJM: 全訳（改訂している場合は最終版と初版からの変更箇所のまとめ）
  - Lancet系、JCO: 簡易版（概要、試験で使用する規約・規準、適格・除外規準、治療、評価項目、エンドポイント、統計的事項）
- 翻訳会社の翻訳では臨床試験の専門用語が適切に訳されていない（ことが多い）
  - エンドポイント、統計的事項、体裁調整はDCが担当

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GPP: Good Publication Practice

CONSORT: Consolidated Standards of Reporting Trials

# Revise対応

- 研究事務局とDCの取りまとめ役で対応
  - 研究事務局: コメントに対する回答と本文追記・修正案の初稿作成
  - DC取りまとめ: review, 統計的事項に関するコメントへの回答・追加解析が必要な場合は統計部門で対応
- Journal別の特徴
  - Lancet系: 4-6人, 7-10コメント/人 (Fast-trackの場合は数日の期限で対応が必要)
  - JCO: 3-4人, 6-10コメント/人
  - NEJM: 2-3人, 3-4コメント/人

# Accept後（proof check）

- NEJMやLancet系は大幅にリライト
  - Proof checkの段階で追加解析の要求
    - %、分母、P値の追記
  - 間違った書き換え
- 投稿通りの内容でもproof checkで気づく間違いもある

- Proof checkも重要！
- 掲載されるまでは気を引き締めて対応を！

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  - CONSORT etc. 報告のためのガイドライン 出版倫理のガイドライン

ICMJE: International Committee of Medical Journal Editors

GPP: Good Publication Practice

CONSORT: Consolidated Standards of Reporting Trials

# 学術出版に関する歴史

|       |                                                                                                                                         |                                                                                           |
|-------|-----------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------|
| 1957年 | JAMAが論文にabstract掲載を慣習化<br>Abstractで読むべき論文の選別が可能になる                                                                                      | 科学分野の発展に伴い論文数が増加                                                                          |
| 1968年 | ワシントン大学の医師の秘書さんが、rejectされた論文を他の学術誌に投稿するために書き換えを依頼される→作業が大変であり投稿規定の統一の要望をNEJM、JAMAなどに投書                                                  |                                                                                           |
| 1979年 | Vancouver group (後のICMJE) より統一投稿規定 (Uniform Requirements for Manuscripts Submitted to Biomedical Journals) 公表                           |                                                                                           |
| 1984年 | NEJMが利益相反に関する声明を発表                                                                                                                      |                                                                                           |
| 1987年 | Annals of Internal Medicine が構造化抄録を紹介                                                                                                   |                                                                                           |
| 1997年 | CONSORT声明公表                                                                                                                             | Food and Drug Administration Modernization Act (FDAMA, FDA近代化法)<br>新規薬剤の臨床試験において臨床試験登録が必要 |
| 2000年 |                                                                                                                                         | ClinicalTrials.gov運用開始                                                                    |
| 2003年 | GPP guidelines公表                                                                                                                        |                                                                                           |
| 2004年 | ICMJE統一投稿規定改訂<br>臨床試験登録を投稿の要件に追加                                                                                                        |                                                                                           |
| 2005年 |                                                                                                                                         | UMIN-CTR運用開始 (日本)                                                                         |
| 2007年 |                                                                                                                                         | Food and Drug Administration Amendments Act of 2007 (FDA改正法)<br>臨床試験登録、結果の公表の義務化          |
| 2010年 | CONSORT2010声明<br>“ICMJE推奨”と改名 (Recommendations for Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals ) |                                                                                           |
| 2013年 |                                                                                                                                         | 欧米の製薬企業よりIPD*の公開・共有が行われるようになる                                                             |
| 2016年 | ICMJE推奨改訂<br>IPDの公開・共有に関する陳述を投稿条件として提案                                                                                                  | * IPD: Individual Patient Data                                                            |

参考文献：トム・ラングの医学論文「執筆・出版・発表」実践ガイド 14

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- 論文投稿の際に知っておくべき各種ガイドライン
  - ICMJE recommendations / GPP guidelines
    - Key words: ①著者資格、②研究貢献者、③利益相反、④重複出版、⑤臨床試験登録、⑥臨床試験データの共有
  - CONSORT etc.

# 出版倫理のガイドライン

## ICMJE recommendations

- 医学雑誌における学術研究の実施、報告、編集、出版への推奨
- ICMJE加盟雑誌に投稿予定の著者は使用推奨

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### Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals

Updated December 2016

- I. About the Recommendations
  - A. Purpose of the Recommendations
  - B. Who Should Use the Recommendations?
  - C. History of the Recommendations
- II. Roles and Responsibilities of Authors, Contributors, Reviewers, Editors, Publishers, and Owners
  - A. Defining the Role of Authors and Contributors
    1. Why Authorship Matters
    2. Who Is an Author?
    3. Non-Author Contributors
  - B. Author Responsibilities—Conflicts of Interest
    1. Participants
      - a. Authors
      - b. Peer Reviewers
      - c. Editors and Journal Staff
    2. Reporting Conflicts of Interest
  - C. Responsibilities in the Submission and Peer-Review Process
    1. Authors
      - a. Predatory Journals
      - b. Confidentiality
      - c. Timeliness
      - d. Peer Review
    2. Journals
      - a. Confidentiality
      - b. Timeliness
      - c. Peer Review
      - d. Integrity
    3. Peer Reviewers
    - D. Journal Owners and Editorial Freedom
      1. Journal Owners
      2. Editorial Freedom
    - E. Protection of Research Participants
  - III. Publishing and Editorial Issues Related to Publication in Medical Journals
    - A. Corrections and Version Control
    - B. Scientific Misconduct, Expressions of Concern, and Retraction
    - C. Copyright
    - D. Overlapping Publications
      1. Duplicate Submission
      2. Duplicate Publication
      3. Acceptable Secondary Publication
      4. Manuscripts Based on the Same Database
    - E. Correspondence
    - F. Fees
    - G. Supplements, Theme Issues, and Special Series
    - H. Sponsorship of Partnerships
    - I. Electronic Publishing
    - J. Advertising
    - K. Journals and the Media
    - L. Clinical Trial Registration
  - IV. Manuscript Preparation and Submission
    - A. Preparing a Manuscript for Submission to a Medical Journal
      1. General Principles
      2. Reporting Guidelines
      3. Manuscript Sections
        - a. Title Page
        - b. Abstract
        - c. Introduction
        - d. Methods
          - i. Selection and Description of Participants
          - ii. Technical Information
          - iii. Statistics
        - e. Results
        - f. Discussion
        - g. References
          - i. General Considerations
          - ii. Style and Format
        - h. Tables
        - i. Illustrations (Figures)
        - j. Units of Measurement
        - k. Abbreviations and Symbols
      - B. Sending the Manuscript to the Journal
    - I. ABOUT THE RECOMMENDATIONS
      - A. Purpose of the Recommendations
      - ICMJE developed these recommendations to review best practice and ethical standards in the conduct and reporting of research and other material published in medical journals, and to help authors, editors, and others involved in peer review and biomedical publishing create and distribute accurate, clear, reproducible, unbiased medical journal articles. The recommendations may also provide useful insights into the medical editing and publishing process for the media, patients and their families, and general readers.
      - B. Who Should Use the Recommendations?
      - These recommendations are intended primarily for use by authors who might submit their work for publication to ICMJE member journals. Many non-ICMJE journals voluntarily use these recommendations (see [www.icmje.org/journals.html](http://www.icmje.org/journals.html)). The ICMJE encourages that use but has no authority to monitor or enforce it. In all cases, authors should use these recommendations along with individual journals' instructions to authors. Authors should also consult guidelines for the reporting of specific study types (e.g., the CONSORT guidelines for the reporting of randomized trials); see <http://equator-network.org>.
      - Journals that follow these recommendations are encouraged to incorporate them into their instructions to

<http://www.icmje.org/icmje-recommendations.pdf>

## GPP guidelines

- 国際医学出版専門業協会\*が作成
- 企業スポンサーの医学研究結果を公表する際のガイドライン

\*International Society for Medical Publication Professionals (ISMPP)

Annals of Internal Medicine RESEARCH AND REPORTING METHODS

### Good Publication Practice for Communicating Company-Sponsored Medical Research: GPP3

Wendy P. Battist, PhD; Elizabeth Wagner, PhD; Lisa Baltzer, PhD; Angela Cairns; Christopher L. Carswell, MS; Leslie Citrome, MD, MPH; James A. Gurr, PhD; LeVerne A. Mooney, DPH; B. Jane Moore, MS; Teresa Pena, PhD; Carol H. Sannes-Miller, MS; Keith Veitch, PhD; Karen L. Woolley, PhD; and Yvonne E. Yarker, PhD

This updated Good Publication Practice (GPP) guideline, known as GPP3, builds on earlier versions and provides recommendations for individuals and organizations that contribute to the publication of research results sponsored or supported by pharmaceutical, medical device, diagnostics, and biotechnology companies. The recommendations are designed to help individuals and organizations maintain ethical and transparent publication practices and comply with legal and regulatory requirements. These recommendations cover publications in peer-reviewed journals and presentations (oral or poster) at scientific congresses. The International Society for Medical Publication Professionals invited more than 3000 professionals worldwide to apply for a position on the steering committee, or as a reviewer, for this guideline. The GPP2 authors reviewed all applications (n = 241) and assembled an 18-member steering committee that represented 7 countries and a diversity of publication professions and institutions. From the 174 selected reviewers, 94 sent

comments on the second draft, which steering committee members incorporated after discussion and consensus. The resulting guideline includes new sections (Principles of Good Publication Practice for Company-Sponsored Medical Research, Data Sharing, Studies That Should Be Published, and Plagiarism), expands guidance on the International Committee of Medical Journal Editors' authorship criteria and common authorship issues, improves clarity on appropriate author payment and reimbursement, and expands information on the role of medical writers. By following good publication practices (including GPP3), individuals and organizations will show integrity, accountability, and responsibility for accurate, complete, and transparent reporting in their publications and presentations.

Ann Intern Med. 2015;163:461-464. doi:10.7326/M15-0268. www.annals.org  
For author affiliations, see end of text.  
This article was published online first at [www.annals.org](http://www.annals.org) on 11 August 2015.

Incomplete, inaccurate, misleading, or delayed reporting of medical research may result in poorly informed decision making and reduce the efficiency and quality of health care (1). Therefore, scientific and clinical research should be reported in a complete, accurate, balanced, and timely manner. Such research is often initiated by, or involves collaboration with, commercial organizations, such as pharmaceutical, biotechnology, medical device, and diagnostics companies. This updated Good Publication Practice guideline, known as GPP3, is designed primarily to help individuals and organizations maintain ethical practices when they contribute to the communication of this type of research. The principles of GPP3 apply to all research, however, so we expect that this guideline will be applicable to all medical and health care professionals involved in publications.

The GPP guideline, published in 2003 (2) and updated in 2009 (as GPP2) (3), has been widely adopted. In an international survey of almost 500 people involved in publishing industry-sponsored research, more than 90% of respondents said they routinely referred to GPP2, which is a similar proportion to those who reported using International Committee of Medical Journal Editors (ICMJE) guidelines (4). The GPP guidelines have also been endorsed by medical journals (5) and cited in their instructions to authors.

The latest revision, GPP3, reflects changes in the medical publications environment and aims to clarify and strengthen the principles and practices described in earlier versions. This guideline also reflects some important changes from GPP2 (Table).

Throughout the guideline, we use the term "publications" to include the full range of formats published in peer-reviewed journals (for example, original research articles, short reports, reviews, or letters to the editor) and "presentations" to include abstracts, posters, and slides for oral presentations at scientific congresses. "Sponsors" are organizations that provide primary support, which may include funding, for a study. "Publication professionals" are professional medical writers, publication planners, and publication managers, usually working either in or for companies. This guideline does not cover regulatory documents, medical education programs, or marketing or advertising materials, all of which are regulated or accredited by specific national or regional authorities.

#### METHODS

In August 2013, an e-mail invitation was sent to more than 3000 professionals from around the world, including International Society for Medical Publication Professionals (ISMPP) members (n = 1430); persons invited to review GPP2 (n = 288); and a distribution list from the Medical Publishing Insights and Practices initiative that included approximately 1400 investigators, researchers, and journal editors. Candidates were invited to volunteer as members of the GPP3 steering committee or reviewers (or both). Eight GPP2 authors screened the applications (n = 241). Of 118 steering committee applicants, 11 were chosen and joined 7 of the former GPP2 authors to provide a broad range of perspectives (from 7 countries, including employees of pharmaceutical, biotechnology, medical device, and

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<http://www.ismpp.org/gpp3>

# ICMJE: 医学雑誌編集者国際委員会

(International Committee of Medical Journal Editors)

ICMJE INTERNATIONAL COMMITTEE of MEDICAL JOURNAL EDITORS

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Recommendations Conflicts of Interest Journals Following the ICMJE Recommendations About ICMJE News & Editorials

**Recommendations**

Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals\*

Read the ICMJE Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals\*

**統一投稿規定**

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ICMJE Form for Disclosure of Potential Conflicts of Interest

Use the ICMJE Form for Disclosure of Potential Conflicts of Interest to generate a disclosure statement

**利益相反**

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## 会員雑誌

### ANNOUNCEMENTS

ICMJE Announces Requirement for Clinical Trial Data Sharing Statements - June, 2017

READ THE EDITORIAL

SHARE YOUR FEEDBACK

Up-dated ICMJE Recommendations - December, 2016

### Quick Links

- Clinical Trial Registration
- Who is an Author?
- FAQs
- Request to receive an E-mail when the Recommendations are updated.

### About ICMJE

The ICMJE is a small group of general medical journal editors and representatives of selected related organizations working together to improve the quality of medical science and its

### Member Publications & Organizations



NEJM, LANCETも

→ Journals Following the ICMJE Recommendations

臨床試験登録  
著者の規定  
FAQ

# ①著者の資格（4要件）

1. 試験デザイン、データ入手、データ解析、データの解釈のいずれかに実質的な貢献
2. 原稿作成または批判的な推敲への関与
3. 出版原稿の最終承認
4. 研究内容に関する責任を負うことの同意

- 多施設共同研究の場合はグループ名も可能
- 上記4要件すべて満たさなければ著書になれない（すべて満たさない場合は“研究貢献者（Non-Author Contributor）”として謝辞に記載）
- 1の要件を満たすものには2と3の機会をもつべき

## ②研究貢献者 Non-Author Contributor

- 著者の4要件を満たさないが、研究への貢献があるもの（単独の貢献では著者にはなれない）
  - 研究資金の確保
  - 一般的な支援を行った部門長
  - 執筆援助、技術編集、用語編集、校正
- 研究者は役割とともに列記
  - 学術的助言、データ収集、研究デザインの批判的校閲、被験者の提供・ケア、原稿の執筆または編集作業への参加など
- 謝辞に名前を列記することに関して書面の承諾

### ③利益相反 Conflicts of Interest (COI)

- 公表論文に対する信頼性の確保には利益相反への対処が重要
- 利益相反の種類
  - 財政的利害関係（雇用、株式所有、謝礼金など）
  - 個人的関係または競争、学問的競争、知的信念など
- 査読～出版の過程のすべての関係者のうち、役割を果たす場合は、利益相反を開示
- ICMJEの統一書式を用いて報告
  - ICMJEメンバーの雑誌では使用必須
  - その他の雑誌でも採用を推奨

# ICMJE disclosure form

ICMJE INTERNATIONAL COMMITTEE of MEDICAL JOURNAL EDITORS

SAVE

## ICMJE Form for Disclosure of Potential Conflicts of Interest

### Section 1. Identifying Information

1. Given Name (First Name) 2. Surname (Last Name) 3. Date

4. Are you the corresponding author? ☐ Yes ☐ No

5. Manuscript Title

6. Manuscript Identifier

**当該研究に対して著者・所属施設への  
資金提供の有無  
→Fundingの記載と重複の可能性あり**

### Section 2. The Work Under Consideration for Publication

Did you or your institution at any time receive payment or services from a third party (government, commercial, private foundation, etc.) for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc.)?

Are there any relevant conflicts of interest? ☒ Yes ☐ No

If yes, please fill out the appropriate information below. If you have more than one entity press the "ADD" button to add a new row. Excess rows can be removed by pressing the "X" button.

| Name of Institution/Company | Grant?                   | Personal Fees?           | Non-Financial Support?   | Other?                   | Comments |
|-----------------------------|--------------------------|--------------------------|--------------------------|--------------------------|----------|
|                             | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |          |

**財政的利害関係（過去3年間）**

### Section 3. Relevant financial activities outside the submitted work.

Place a check in the appropriate boxes in the table to indicate whether you have financial relationships (regardless of amount of compensation) with entities as described in the instructions. Use one line for each entity; add as many lines as you need by clicking the "Add +" box. You should report relationships that were present during the 36 months prior to publication.

Are there any relevant conflicts of interest? ☒ Yes ☐ No

If yes, please fill out the appropriate information below.

| Name of Entity | Grant?                   | Personal Fees?           | Non-Financial Support?   | Other?                   | Comments |
|----------------|--------------------------|--------------------------|--------------------------|--------------------------|----------|
|                | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |          |

ADD

ICMJE INTERNATIONAL COMMITTEE of MEDICAL JOURNAL EDITORS

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## ICMJE Form for Disclosure of Potential Conflicts of Interest

### Section 4. Intellectual Property -- Patents & Copyrights

Do you have any patents or copyrights?

**特許権、著作権など**

### Section 5. Relationships not covered above

Are there other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what you wrote in the submitted work?

☒ Yes, the following relationships/conditions/circumstances are present (explain below):

☐ No other relationships/conditions/circumstances that present a potential conflict of interest

**その他（個人的関係、学問的競争など）**

### Section 6. Disclosure Statement

Based on the above disclosures, this form will automatically generate a disclosure statement, which will appear in the box below.

**ここをクリック**

Generate Disclosure Statement

**自動的に文章が作成される**

### Evaluation and Feedback

Please visit <http://www.icmje.org/cgi-bin/feedback> to provide feedback on your experience with completing this form.

## ④重複出版 Overlapping Publication

- 多重投稿 Duplicate submission
  - 同じ言語または他の言語のいずれかで同一論文を同時に2つ以上の雑誌に投稿すること
    - 著作権をどこがもつかでもめる
    - 査読、編集、掲載紙面が重複することによるリソースの無駄遣い
    - 例外：公衆衛生上有益と判断される場合
- 多重出版 Duplicate and prior publication
  - すでに出版された論文と大部分が重複する論文を先に出版された論文への明確な言及をせずに掲載すること
  - 以下は対象外
    - 他誌で不採用
    - 学会発表後の内容（投稿時に申告は要）
    - 臨床試験登録への結果報告（投稿時に申告は要）
  - 例外：公衆衛生上有益と判断される場合
- 二次出版 Secondary publication
  - 他誌またはオンラインで掲載された論文をできる限り多くの読者に重要な情報を行き渡らせることを意図したもの
  - その他は、以下の条件を満たせば可
    - 両方の雑誌の編集者から許可あり
    - 初版から1週間以上経過
    - 読者層が異なる
    - 初版のデータ、解釈を忠実に反映
    - 二次出版であることを明示

# 二次出版の例

- 英文論文を和文の雑誌に投稿したい場合  
日本外科学会邦文誌現行投稿規定（抜粋）

## Acceptable secondary publication(容認可能な二重投稿)

ICMJE(International Committee of Medical Journal Editors)は一定の条件を満たす場合、Acceptable secondary publicationとして、これを認めている。投稿論文が以下の条件を満たしており、編集委員長が認めた場合、その投稿論文をsecondary publicationとして査読の対象とする。

- 1) Secondary publicationとは日本語以外の言語で出版されたprimary versionのデータ、解釈に関し、それを忠実に反映して日本文で書かれたものである。
- 2) 筆者は、primary publicationの編集長の同意書を受領する。日本外科学会雑誌の編集長は、primary versionのコピー、別刷または原稿を所有しなくてはならない。
- 3) 出版の優先権は、少なくとも1週間の間隔をあけて、出版することによりprimary versionとして尊重される。
- 4) Secondary versionの論文のタイトルページ脚注には、その論文が全体または一部にかかわらず、出版済みであることを示す必要があり、またprimary versionの論文を参考にしたことを明確に記載する。脚注については、以下の文例を使用すること。「この論文は既に掲載された論文である。(題名、雑誌名、発表年、巻号、頁数)」

[https://www.jssoc.or.jp/journal/jss\\_journal/jrn\\_journal\\_guideline.html](https://www.jssoc.or.jp/journal/jss_journal/jrn_journal_guideline.html)

二次出版に関する雑誌の投稿規定を要確認

# ⑤臨床試験登録が掲載要件に追加

(2004年9月ICMJEから声明)

- なぜ？
  - 2000年よりClinicalTrials.gov運用開始
    - 公表バイアスをなくするため
- 登録が必要な「臨床試験」の定義
  - 対象患者を前向きに登録する研究
  - 介入とアウトカムの因果関係を検討する研究
- 登録内容
  - 臨床試験の方法論
  - 国際的臨床試験登録プラットフォームで定められた20項目
    - 試験名、対象、試験治療、エンドポイント、予定登録数、登録開始日、実施組織、問い合わせ先など
  - 結果のサマリー
    - 2007年FDA改正法に対応したものは過去の公表とはみなさない(多重出版ではない)

# ⑥臨床試験データの共有

## Clinical Trial Data Sharing (CTDS)

- 背景
  - 向精神薬などの臨床試験で透明性が問題となる事例あり
  - 2013年7月 欧米の製薬企業によりIPDの公開・共有が行われるようになる
  - 2016年1月 ICMJEがIPDの公開・共有に関する陳述を投稿条件として提案
- なぜ？
  - リスクを負って試験に参加した患者から得られた情報は社会の共有財産 (pros)
  - 実施可能性への懸念 (cons)
- CTDSへの対応要
  - 2018年7月1日以降に臨床試験の論文を投稿
    - Data sharingに関するstatementが必要
  - 2019年1月1日以降に開始する臨床試験
    - プロトコールにData sharingに関する規定を設け、臨床試験登録に含める
- 記載/登録内容（詳細は次項）

Table. Examples of Data Sharing Statements That Fulfill These ICMJE Requirements\*

|                                                                                                 | Example 1                                                                                              | Example 2                                                                                                                                                                                                   | Example 3                                                                                                                                                                                                                                                                                                                             | Example 4      |
|-------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------|
| Will individual participant data be made available in a public repository or data dictionaries? | Yes                                                                                                    | Yes                                                                                                                                                                                                         | Yes                                                                                                                                                                                                                                                                                                                                   | No             |
| What data in particular?                                                                        | All of the individual participant data collected during the trial, after deidentification.             | Individual participant data that underlie the results reported in this article, after deidentification (text, tables, figures, and appendices).                                                             | Individual participant data that underlie the results reported in this article, after deidentification (text, tables, figures, and appendices).                                                                                                                                                                                       | Not available  |
| What other documents?                                                                           | Study Protocol, Statistical Analysis Plan, Informed Consent Form, Clinical Study Report, Analytic Code | Study Protocol, Statistical Analysis Plan, Analytic Code                                                                                                                                                    | Study Protocol                                                                                                                                                                                                                                                                                                                        | Not available  |
| For how long?                                                                                   | Immediately following publication. No end date.                                                        | Beginning 3 months and ending 5 years following article publication.                                                                                                                                        | Beginning 9 months and ending 36 months following article publication.                                                                                                                                                                                                                                                                | Not applicable |
| With whom?                                                                                      | Anyone who wishes to access the data.                                                                  | Researchers who provide a methodologically sound proposal.                                                                                                                                                  | Investigators whose proposed use of the data has been approved by an independent review committee ("learned intermediary") identified for this purpose.                                                                                                                                                                               | Not applicable |
| By what mechanism will data be made available?                                                  | Any purpose.                                                                                           | To achieve aims in the approved proposal.                                                                                                                                                                   | For individual participant data meta-analysis.                                                                                                                                                                                                                                                                                        | Not applicable |
| By what mechanism will data be made available?                                                  | Data are available indefinitely at ( <i>Link to be included</i> ).                                     | Proposals should be directed to xxx@yyy. To gain access, data requestors will need to sign a data access agreement. Data are available for 5 years at a third party website ( <i>Link to be included</i> ). | Proposals may be submitted up to 36 months following article publication. After 36 months the data will be available in our University's data warehouse but without investigator support other than deposited metadata. Information regarding submitting proposals and accessing data may be found at ( <i>Link to be provided</i> ). | Not applicable |

\* These examples are meant to illustrate a range of, but not all, data sharing options.

[http://www.icmje.org/news-and-editorials/data\\_sharing\\_june\\_2017.pdf](http://www.icmje.org/news-and-editorials/data_sharing_june_2017.pdf)

# 記載例

(日本製薬工業協会「臨床試験の個別被験者データの共有」を参照し、演者が和訳)

|                   | Example 1                   | Example 4 |
|-------------------|-----------------------------|-----------|
| IPDは利用できる？        | 利用可                         | 利用不可      |
| どのデータが共有できる？      | 非特定化*後、研究期間のすべてのデータを利用可     | 利用不可      |
| データ以外に利用できる文書は何か？ | プロトコール、解析計画書、IC文書、CRF、解析コード | 利用不可      |
| いつからいつまでが利用可能か？   | 結果の公表直後から永久利用可              | 当てはまらない   |
| 誰が利用可能か？          | データにアクセスできるすべての利用者          | 当てはまらない   |
| 利用目的は何か？          | いかなる目的でも可                   | 当てはまらない   |
| データの入手方法は？        | リンク先から制限なしで入手可              | 当てはまらない   |

\*非特定化（De-identification）：あるデータの対象が特定の個人に結びつかないようにすること

# 記載例

(日本製薬工業協会「臨床試験の個別被験者データの共有」を参照し、演者が和訳)

|                   | Example 2                    | Example 3                    |
|-------------------|------------------------------|------------------------------|
| IPDは利用できる？        | 利用可                          | 利用可                          |
| どのデータが共有できる？      | 本文、図表、別表に示された結果のIPDを非特定化後利用可 | 本文、図表、別表に示された結果のIPDを非特定化後利用可 |
| データ以外に利用できる文書は何か？ | プロトコール、解析計画書、IC文書、CRF、解析コード  | プロトコール                       |
| いつからいつまでが利用可能か？   | 結果の公表の3か月後から5年後まで            | 結果の公表の3か月後から3年後まで            |
| 誰が利用可能か？          | 科学的価値のある計画を提出してきた研究者         | 外部の審査委員会で承認された計画を提出してきた研究者   |
| 利用目的は何か？          | 審査委員会で承認された計画                | IPDを利用したメタアナリシス              |
| データの入手方法は？        | 連絡先とデータ利用に関する合意書について記載       | 計画の提出先等の情報に関する記載             |

# GPP guidelines

- 基本的にはICMJE recommendationsと同じ
- ICMJE recommendationsとの違い
  - スポンサー企業と研究者の関係に関する記載が含まれる
  - 著者資格に関する詳細な解説記載あり
  - 投稿までの期間について言及あり（既承認薬であれば12-18か月）
  - “Professional medical writer”に関する記載

詳細は原著をご参照

# 本日の内容

- JCOG試験の論文がpublishされるまでの道のり
  - 初稿作成～投稿
  - Revise対応～accept～掲載
- 論文投稿の際に知っておくべき各種ガイドライン
  - ICMJE recommendations / GPP guideline  
Key words: 著者資格、研究貢献者、利益相反、重複出版、臨床試験登録、臨床試験データの共有
  - CONSORT etc.

# 報告のためのガイドライン

- EQUATOR Network <http://www.equator-network.org/>
  - CONSORT: ランダム化試験 <http://www.consort-statement.org/>
  - STROBE: 観察研究 <https://www.strobe-statement.org/>
  - PRISMA: システマティックレビュー, メタアナリシス <http://www.prisma-statement.org/>
  - STARD: 診断精度の研究 <http://www.stard-statement.org/>

- 他の研究者、編集者が研究の評価をする際に有用
- 著者が研究の記述をする際に有用

# CONSORT 2010 声明

表 ランダム化比較試験を報告する際に含まれるべき情報の CONSORT 2010 チェックリスト\*  
CONSORT 2010 checklist of information to include when reporting a randomized trial

| 章/トピック<br>(Section/Topic)                                           | 項目番号<br>(Item No)                                       | チェックリスト項目<br>(Checklist Item)                                                                                                          | 報告頁<br>(Reported on page No) |
|---------------------------------------------------------------------|---------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------|------------------------------|
| タイトル・抄録<br>(Title and Abstract)                                     | 1a                                                      | タイトルにランダム化比較試験であることを記載。                                                                                                                |                              |
|                                                                     | 1b                                                      | 試験デザイン (trial design)、方法 (method)、結果 (result)、結論 (conclusion) の構造化抄録 (詳細は「雑誌および会議録でのランダム化試験の抄録に対する CONSORT 声明」 <sup>21, 30</sup> を参照)。 |                              |
| はじめに (Introduction)<br>背景・目的<br>(Background and Objective)          | 2a                                                      | 科学的背景と論議 (rationale) の説明。                                                                                                              |                              |
|                                                                     | 2b                                                      | 特定の目的または仮説 (hypothesis)。                                                                                                               |                              |
| 方法 (Method)<br>試験デザイン (Trial Design)                                | 3a                                                      | 試験デザインの記述 (並行群間、要因分析など)、割付け比を含む。                                                                                                       |                              |
|                                                                     | 3b                                                      | 試験開始後の方法上の重要な変更 (適格基準 eligibility criteria など) とその理由。                                                                                  |                              |
|                                                                     | 参加者 (Participant)                                       | 4a 参加者の適格基準 (eligibility criteria)。                                                                                                    |                              |
|                                                                     |                                                         | 4b データが収集されたセッティング (setting) と場所。                                                                                                      |                              |
|                                                                     | 5                                                       | 再現可能となるような詳細な各群の介入。実際にいつどのように実施されたかを含む。                                                                                                |                              |
|                                                                     | アウトカム (Outcome)                                         | 6a 事前に特定され明確に定義された主要・副次的アウトカム評価項目。いつどのように評価されたかを含む。                                                                                    |                              |
|                                                                     |                                                         | 6b 試験開始後のアウトカムの変更とその理由。                                                                                                                |                              |
|                                                                     | 症例数 (Sample size)                                       | 7a どのように目標症例数が決められたか。                                                                                                                  |                              |
|                                                                     |                                                         | 7b あてはまる場合には、中間解析と中止基準の説明。                                                                                                             |                              |
|                                                                     | ランダム化 (Randomization)<br>順序の作成<br>(Sequence generation) | 8a 割振り (allocation) 順序を作成 (generate) した方法。                                                                                             |                              |
|                                                                     |                                                         | 8b 割振りのタイプ: 制限の詳細 (ブロック化、ブロックサイズなど)。                                                                                                   |                              |
|                                                                     | 9                                                       | ランダム割振り順序の実施に用いられた機構 (番号付き容器など)、各群の割付けが終了するまで割振り順序が隠蔽されていたかどうかの記述。                                                                     |                              |
| ランダム化 (Randomization)<br>実施 (Implementation)<br>ブラインディング (Blinding) | 10                                                      | 誰が割振り順序を作成したか、誰が参加者を組入れ (enrollment) たか、誰が参加者を各群に割付けた (assign) か。                                                                      |                              |
|                                                                     | 11a                                                     | ブラインド化されていた場合、介入に割付け後、誰がどのようにブラインド化されていたか (参加者、介入実施者、アウトカムの評価者など)。                                                                     |                              |
|                                                                     |                                                         | 11b 関連する場合、介入の類似性の記述。                                                                                                                  |                              |
|                                                                     | 統計学的手法<br>(Statistical method)                          | 12a 主要・副次的アウトカムの群間比較に用いられた統計学的手法。                                                                                                      |                              |
|                                                                     |                                                         | 12b サブグループ解析や調整解析のような追加的解析の手法。                                                                                                         |                              |
| 結果 (Results)<br>参加者の流れ<br>(Participant flow)<br>(フローチャートを強く推奨)      | 13a                                                     | 各群について、ランダム割付けされた人数、意図された治療を受けた人数、主要アウトカムの解析に用いられた人数の記述。                                                                               |                              |
|                                                                     | 13b                                                     | 各群について、追跡不能例とランダム化後の除外例を理由とともに記述。                                                                                                      |                              |
|                                                                     | 募集 (Recruitment)                                        | 14a 参加者の募集期間と追跡期間を特定する日付。                                                                                                              |                              |
|                                                                     |                                                         | 14b 試験が終了または中止した理由。                                                                                                                    |                              |
|                                                                     | 15                                                      | 各群のベースラインにおける人口統計学的 (demographic)、臨床的な特性を示す表。                                                                                          |                              |
|                                                                     | 16                                                      | 各群について、各解析における参加者数 (分母)、解析が元の割付け群によるものであるか。                                                                                            |                              |
| 結果 (Results)<br>アウトカムと推定<br>(Outcome and estimation)                | 17a                                                     | 主要・副次的アウトカムのそれぞれについて、各群の結果、介入のエフェクト・サイズの推定とその精度 (95% 信頼区間など)。                                                                          |                              |
|                                                                     | 17b                                                     | 2項アウトカムについては、絶対エフェクト・サイズと相対エフェクト・サイズの両方を記載することが推奨される。                                                                                  |                              |
|                                                                     | 18                                                      | サブグループ解析や調整解析を含む、実施した他の解析の結果。事前に特定された解析と探索的解析を区別する。                                                                                    |                              |
| 結果 (Results)<br>補助的解析<br>(Ancillary analysis)<br>害 (Harm)           | 19                                                      | 各群のすべての重要な害 (harm) または意図しない効果 (詳細は「ランダム化試験における害のよりよい報告: CONSORT 声明の拡張」 <sup>20</sup> を参照)。                                             |                              |
|                                                                     | 考察 (Discussion)<br>限界 (Limitation)                      | 20 試験の限界、可能性のあるバイアスや精度低下の原因、関連する場合は解析の多重性の原因を記載。                                                                                       |                              |
|                                                                     |                                                         | 21 試験結果の一般化可能性 (外的妥当性、適用性)。                                                                                                            |                              |
| 考察 (Discussion)<br>解釈 (Interpretation)                              | 22                                                      | 結果の解釈、有益性と有害性のバランス、他の関連するエビデンス。                                                                                                        |                              |
| その他の情報<br>(Other information)                                       | 登録 (Registration)                                       | 23 登録番号と試験登録名。                                                                                                                         |                              |
|                                                                     |                                                         | 24 可能であれば、完全なプロトコルの入手方法。                                                                                                               |                              |
|                                                                     | 資金提供者 (Funding)                                         | 25 資金提供者と他の支援者 (薬剤の供給者など)、資金提供者の役割。                                                                                                    |                              |
|                                                                     |                                                         |                                                                                                                                        |                              |

## RCTの結果報告の際に必要なチェックリスト (25項目) とフローチャート

- 投稿の際の別添資料 (Lancet)
- チェックリストの情報とフローチャートを本文に記載 (NEJM)

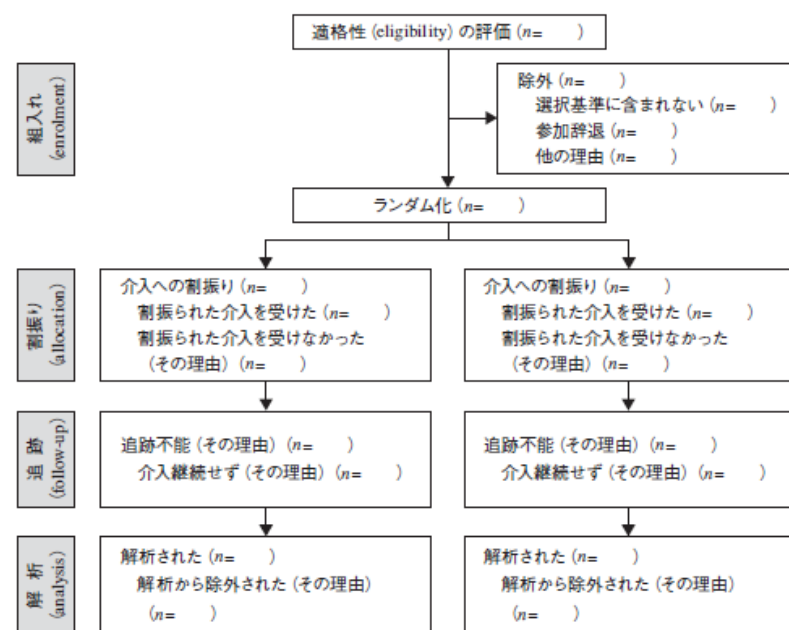


図 2 群間並行ランダム化比較試験の各段階の過程を示すフローチャート (組入れ、介入への割振り、追跡、データ解析)  
Flow diagram of the progress through the phases of a parallel randomized trial of two groups (that is, enrolment, intervention allocation, follow-up, and data analysis)

# Take home message

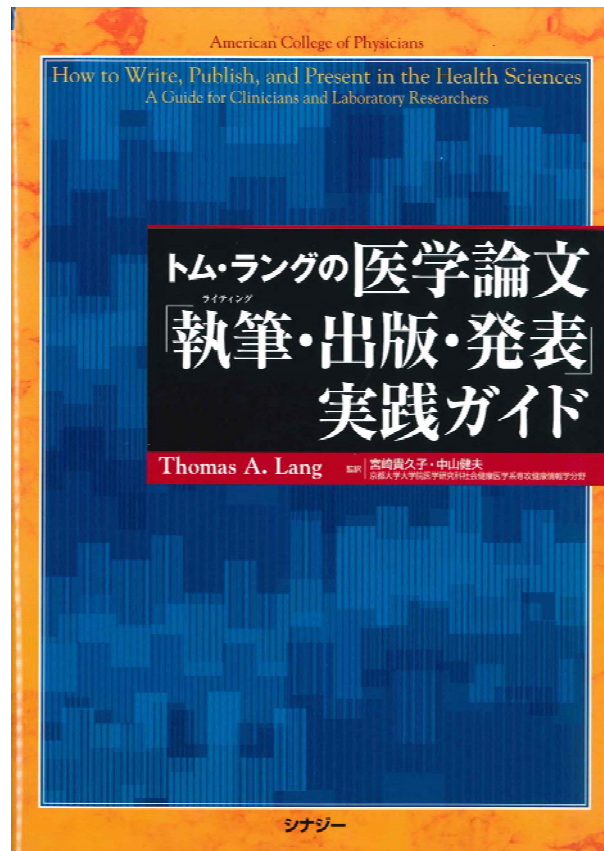
- 結果の公表（論文公表）まで質の担保が重要
  - 研究者のみではなく、支援部門の責務としてreviewする
- 著者になる場合の心がけ
  - 投稿規定に従った初稿作成
  - 雑誌に掲載されるまで気を抜かない（Proof checkも重要！）
- 共著者になる場合の心がけ
  - 責任は筆頭でも共著者でも同じ
  - 推敲にもしっかり貢献をする
- 臨床試験データの共有
  - 現時点ではデータ共有が必須ではない
  - 提供を求められた際の対応については要検討

# 参考文献

- ICMJE
  - 医学雑誌における推奨 <http://www.icmje.org/>
  - Disclosure form <http://www.icmje.org/recommendations/browse/>  
<http://www.icmje.org/conflicts-of-interest/>
- ISMPP <http://www.ismpp.org/>
  - GPP guideline (GPP3) <http://www.ismpp.org/gpp3>
- EQUATOR Network <http://www.equator-network.org/>
  - CONSORTなど
- Data sharing
  - 臨床試験の個別被験者データの共有（日本製薬工業協会）  
<http://www.jpma.or.jp/medicine/shinyaku/tiken/allotment/ctds.html>

# 参考文献

トム・ラングの医学論文「執筆・出版・発表」実践ガイド



臨床研究と疫学研究のための国際ルール集 (Part 2)

