### Additional file 1: Details of the randomised trials included in the review

<table>
<thead>
<tr>
<th>Study</th>
<th>Design Treatments</th>
<th>Results</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bowen et al. Clin Gastroenterol Hepatol 2005 3: 1075-1082</td>
<td>Post-hoc analysis of two RCTs with ibuprofen as control. Cr51-labelled RBC to measure faecal erythrocyte excretion in controlled conditions over 28 days</td>
<td>Placebo run in average faecal blood loss was 0.36 mL/day. No subject on placebo had &gt;2 mL/day, with daily mean of 0.7 mL/day (±0.4 SD). On ibuprofen the mean daily blood loss was 2.6 mL/day (±3.2 SD). 28-day blood loss averaged 20 mL for placebo and 71 mL for ibuprofen, but was between 100 and 300 mL in 5 patients</td>
<td>Note that patients here are second analysis of two RCTs below (Hunt, 2000, 2003). Individual daily blood loss on ibuprofen with micro bleeding episodes, episodic in nature. All had &gt;2 mL/day average loss. 27/31 on ibuprofen had from 2-7 episodes of &gt;3 mL/day, 5 subjects 4 episodes &gt;2 and &lt;3mL/day. Nine subjects had maximum blood loss &gt;10 mL/day, with about 70 mL/day in two 5/31 lost &gt;3.5 mL/day on average over 28 days 2/31 lost &gt;6 mL/day on average over 28 days</td>
</tr>
<tr>
<td>Hunt et al. Aliment Pharmacol Ther 2003 17: 201-210</td>
<td>Cr51-labelled RBC to measure faecal erythrocyte excretion in controlled conditions over 28 days</td>
<td>Average daily blood loss end week 4: Placebo 0.9 mL/day Ibuprofen 2,400 mg daily 3.4 mL/day Etoricoxib 120 mg daily 0.9 mL/day</td>
<td>Mean values taken from figure. No dispersion data available</td>
</tr>
<tr>
<td>Hunt et al. Am J Med 2000 109: 201-206</td>
<td>Cr51-labelled RBC to measure faecal erythrocyte excretion in controlled conditions over 28 days</td>
<td>Average daily blood loss at baseline was about 0.4 mL/day Over weeks 2-4: Placebo 0.7 mL/day Rofecoxib 0.8 mL/day Rofecoxib 0.8 mL/day Ibuprofen 1.8 mL/day</td>
<td>Mean values taken from table. No dispersion data available</td>
</tr>
</tbody>
</table>
Cr51-labelled RBC to measure faecal erythrocyte excretion in controlled conditions over 4-7 days of 7 days treatment in two crossover groups randomised for addition of clopidrogel

- Both groups (n=15) received placebo followed by naproxen 500 mg daily
- Average daily blood loss at baseline was about 0.3 mL/day
- Over last 3 or 4 days of study period:
  - Group 1: Placebo 0.4 (±0.4 SD) mL/day
  - Naproxen 1.1 (±0.6) mL/day
- Group 2:
  - Placebo 0.3 (±0.2 SD) mL/day
  - Naproxen 1.9 (±1.5) mL/day
- Maximum daily blood loss with naproxen was 2.4 mL/day in group 1 and 5.8 mL/day in group 2

Another treatment period also examined the effects of clopidrogel. Without clopidrogel mean daily blood loss was 1.8 mL/day (maximum 5.6 mL/day). With clopidrogel mean daily blood loss was 6.8 mL/day (maximum 28 mL/day).

Cr51-labelled RBC to measure faecal erythrocyte excretion in controlled conditions over 2 weeks in a crossover study

- Patients with osteoarthritis (mean age 69 years - range 61-83 years) 19 male, 4 female
- No treatment (n=23)
- Diclofenac 100 mg daily (n=21)
- Naproxen 750 mg daily (n=19)
- Piroxicam 20 mg daily (n=21)
- Average daily blood loss over 3 days at end of treatment
  - No treatment 0.3 (±0.1 SEM) mL/day
  - Diclofenac 100 mg daily 0.5 (±0.2) mL/day
  - Naproxen 750 mg daily 2.8 (±2.2) mL/day
  - Piroxicam 20 mg daily 1.2 (±0.6) mL/day
- Two upper GI bleeding events (diclofenac, piroxicam) and one lower GI bleeding event (diclofenac) occasioned withdrawals

Cr51-labelled RBC to measure faecal erythrocyte excretion in controlled conditions over 28 days

- Healthy male volunteers aged 19-34 years
- Placebo (n=13)
- Meloxican 7.5 mg daily (n=13)
- Meloxican 15 mg daily (n=13)
- Piroxicam 20 mg daily (n=12)
- Baseline values averaged 0.2 mL/day, all 0.5 mL/day or less
- Average daily blood loss days 1-28:
  - Placebo 0.6 (±0.4 SD) mL/day
  - Meloxican 7.5 mg daily 0.8 (±0.5) mL/day
  - Meloxican 15 mg daily 0.9 (±0.7) mL/day
  - Piroxicam 20 mg daily 2.0 (±4.1) mL/day
- Maximum average daily blood loss was 1.9, 2.1, 2.7 and 15 mL daily
- Blood loss tended to be similar for each of four weeks of treatment
- 6/12 patients taking piroxicam were withdrawn due to clinically relevant mucosal damage on endoscopy
<table>
<thead>
<tr>
<th>Study</th>
<th>Cr51-labelled RBC to measure faecal erythrocyte excretion in controlled conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>(trial 1)</td>
<td>Healthy volunteers aged 19-36 years (17 male, 3 female)</td>
</tr>
<tr>
<td>R = 1</td>
<td>DB = 0</td>
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<tr>
<td>W = 1</td>
<td>QS = 2</td>
</tr>
<tr>
<td>Placebo</td>
<td>Plain aspirin 325 mg daily</td>
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<tr>
<td>17 completers; baseline blood loss 0.5 (±0.1 SEM) mL/day</td>
<td>Enteric coated aspirin 325 mg daily (±0.1) mL/day</td>
</tr>
</tbody>
</table>

Average daily blood loss based on 72-hour stool collection at end of treatment:
- Plain aspirin 325 mg daily: 1.8 (±0.4) mL/day
- Enteric coated aspirin 325 mg daily: 1.0 mL/day

No difference between shorter and longer term aspirin consumption for faecal blood loss.

<table>
<thead>
<tr>
<th>Study</th>
<th>Cr51-labelled RBC to measure faecal erythrocyte excretion in controlled conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>(trial 2)</td>
<td>Healthy volunteers aged 21-56 years (38 male, 2 female)</td>
</tr>
<tr>
<td>R = 1</td>
<td>DB = 0</td>
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<tr>
<td>W = 1</td>
<td>QS = 2</td>
</tr>
<tr>
<td>Placebo (n=15)</td>
<td>Plain aspirin 325 mg daily (n=15)</td>
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<tr>
<td>Enteric coated aspirin 325 mg daily (n=15)</td>
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</tbody>
</table>
| Baseline values averaged 0.5 mL/day | Average daily blood loss days over last 3 days:
- Placebo: 0.4 (±0.2 SD) mL/day
- Aspirin 3,900 mg daily: 8.4 (±4.2) mL/day
- Bromfenac 300 mg daily: 2.1 (±1.1) mL/day

Maximum individual daily faecal blood loss about 3 mL/day with bromfenac, 19 mL/day with aspirin

9/13 on aspirin had daily blood loss >5 mL/day
3/13 on aspirin had daily blood loss >10 mL/day
<table>
<thead>
<tr>
<th>Study</th>
<th>RBC Labeling Method</th>
<th>Baseline Faecal Blood Loss</th>
<th>Average Daily Blood Loss Over Last 4 Days of Ibuprofen Administration</th>
<th>Mucolobemide Made No Difference to Faecal Blood Loss or Ibuprofen Kinetics. Randomisation and Blinding Was Not by Ibuprofen Use, So Inclusion of This Trial Is Questionable</th>
</tr>
</thead>
<tbody>
<tr>
<td>Güntert et al. Psychopharmacology 1992 106: S40-S42 (Duplicate)</td>
<td>Cr51-labelled RBC to measure faecal erythrocyte excretion in controlled conditions over 7 days. Randomisation was to moclobemide or placebo, with ibuprofen 1,800 mg introduced on day 8-14 in both groups (12 per group)</td>
<td>Baseline faecal blood loss 0.4 mL/day</td>
<td>Ibuprofen + placebo 1.5 (±1.0 SD) mL/day Ibuprofen + moclobemide 1.3 (±0.6) mL/day</td>
<td>Moclobemide made no difference to faecal blood loss or ibuprofen kinetics. Randomisation and blinding was not by ibuprofen use, so inclusion of this trial is questionable</td>
</tr>
<tr>
<td>Güntert et al. Drug Metab Drug Interact 1991 10: 307-322</td>
<td>Healthy male volunteers aged 19-40 years (n=24)</td>
<td>Average daily blood loss over last 4 days of ibuprofen administration:</td>
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<tr>
<td>Warrington et al. Postgraduate Medical J 1990 66: 622-626</td>
<td>Cr51-labelled RBC to measure faecal erythrocyte excretion in controlled conditions over 28 days</td>
<td>Median daily blood loss days over last 7 days:</td>
<td>Placebo 0.6 mL/day (maximum 13 mL/day) Lornoxicam 0.8 mL/day (maximum 2.7 mL/day) Indomethacin 1.1 mL/day (maximum 2.1 mL/day)</td>
<td>No dispersion given 1/15 on placebo had daily blood loss &gt;10 mL/day Individual patient data available</td>
</tr>
<tr>
<td>Patoia et al. Eur J Clin Pharmacol 1989 36: 599-604</td>
<td>Healthy young volunteers (12 male, 9 female)</td>
<td>Baseline faecal blood loss 0.3 mL/day</td>
<td>Mean daily blood loss days over last 7 days:</td>
<td>Steady increase with piroxicam over 28 days, but 4/7 withdrew over the period with adverse events. Large increases in faecal blood loss in second and third weeks also. In first week mean blood loss 0.5, 1.6 and 1.0 mL/day respectively At least one patinet on piroxicam must have had daily blood loss &gt;5 mL/day</td>
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<tr>
<td>Placebo (n=7)</td>
<td>Piroxicam 20 mg daily (n=7)</td>
<td>Placebo 0.4 (±0.2 SEM) mL/day Piroxicam 4.1 (±2.6) mL/day Piroxicam beta-cyclodextrin 1.2 (±0.4) mL/day</td>
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<tr>
<td>Study</td>
<td>Study Details</td>
<td>Results</td>
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<td>-------------------------------------------------------------------------------</td>
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<tr>
<td>Lynch et al. Aust NZ Med J 1989 19: 89-96</td>
<td>Patients with osteoarthritis aged 18 to 75 years (14 male, 26 female)</td>
<td>Baseline faecal blood loss 0.7 mL/day (maximum 1.4 mL/day)</td>
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<td>Buffered aspirin 4,000 mg daily (N=22)</td>
<td>Average daily blood loss over last 4 days of aspirin administration:</td>
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<tr>
<td></td>
<td>Enteric coated aspirin 3,900 mg daily (n=18)</td>
<td>Buffered aspirin 2.2 mL/day (maximum 6.6 mL/day)</td>
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<tr>
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<td>Enteric coated 3.5 mL/day (maximum 11 mL/day)</td>
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<td>During final week:</td>
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<td>1/18 enteric coated aspirin had blood loss &gt;10 mL/day</td>
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<tr>
<td></td>
<td></td>
<td>1/18 buffered aspirin had blood loss &gt;5 mL/day</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Study</th>
<th>Study Details</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lussier et al. J Clin Pharmacol 1989 29: 225-229</td>
<td>Healthy male volunteers aged 18-32 years (mean 23 years)</td>
<td>Baseline faecal blood loss 0.3 mL/day</td>
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<tr>
<td></td>
<td>Placebo (n=10)</td>
<td>Average daily blood loss over last 7 days of treatment:</td>
</tr>
<tr>
<td></td>
<td>Aspirin 3,600 mg daily (n=10)</td>
<td>Placebo 1.2 (±2.2 ?SD) mL/day</td>
</tr>
<tr>
<td></td>
<td>Nabumetone 2,000 mg daily (n=10)</td>
<td>Aspirin 17 (±2.2) mL/day</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nabumetone 1.6 (±2.2) mL/day</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Note that dispersion values are not stated as SD or SEM, and that identical values for each treatment over several weeks and different means suggests the figures given may be mistaken.</td>
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<tr>
<td></td>
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<td>Steady increase in daily blood loss with aspirin over three weeks</td>
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<td>Assumed that with mean blood loss 17 mL/day, at least 5/10 were over 10, and 7/10 over 5 mL/day</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Study</th>
<th>Study Details</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aabakken et al. Scand J Gastroenterol 1989 24: 1007-1013</td>
<td>Healthy male volunteers aged 20-52 years (mean 24 years)</td>
<td>Baseline faecal blood loss 0.5 mL/day</td>
</tr>
<tr>
<td></td>
<td>Naproxen 750 mg daily (n=16)</td>
<td>Average daily blood loss over 7 days of treatment:</td>
</tr>
<tr>
<td></td>
<td>Oxindanac 600 mg daily (n=16)</td>
<td>Naproxen 1.6 (maximum 3.5) mL/day</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Oxindanac 1.3 (maximum 1.9) mL/day</td>
</tr>
</tbody>
</table>
R = 1
DB = 2
W = 1
QS = 4
Cr51-labelled RBC to measure faecal erythrocyte excretion in controlled conditions over 14 days
Healthy male volunteers aged 35-67 years
Indomethacin Continus 150 mg daily (n=6)
Indomethacin R 150 mg daily (n=6)
Baseline faecal blood loss 0.6 mL/day
Average daily blood loss over last week of treatment:
Indomethacin Continus 2.0 (±0.9 SD) mL/day
Indomethacin R 3.5 (±3.6) mL/day
At end of therapy, 1/12 had daily blood loss >5 mL/day
Mean values after one week were similar, but mainly due to individuals with high blood loss

R = 1
DB = 0
W = 1
QS = 2
Cr51-labelled RBC to measure faecal erythrocyte excretion in controlled conditions over 28 days
Healthy male volunteers aged 18-34 years
Tiaprofic acid tablets 600 mg daily (n=7)
Tiaprofic acid capsules 600 mg daily (n=10)
Indomethacin 75 mg daily (n=10)
Baseline faecal blood loss 0.2 mL/day
Average daily blood loss over fourth week of treatment:
Tiaprofic acid tablets 0.7 mL/day
Tiaprofic acid capsules 0.4 mL/day
Indomethacin 0.9 mL/day
Mean values during second week of treatment were similar
All had maximum blood loss of below 5 mL/day

R = 1
DB = 0
W = 1
QS = 2
Cr51-labelled RBC to measure faecal erythrocyte excretion in controlled conditions over 7 days in a crossover study.
Randomisation was to sucralfate or placebo, with aspirin 4,000 mg daily
Healthy male volunteers aged 20-45 years (n=16)
Baseline faecal blood loss 0.4 mL/day
Average daily blood loss over last 3 days:
Aspirin + placebo 9.6 (±1.8 SEM) mL/day
Aspirin + Sucrelfate 7.2 (±1.6) mL/day
Individual mean daily blood loss of >10 mL/day in 6/16 on aspirin + placebo alone (maximum 25 mL/day), and 4/16 on aspirin + sucralfate
Individual mean daily blood loss of >5 mL/day in 10/16 on aspirin + placebo alone, and 8/16 on aspirin + sucralfate

R = 1
DB = 0
W = 1
QS = 2
Cr51-labelled RBC to measure faecal erythrocyte excretion in controlled conditions over 14 days
Healthy male volunteers aged 21-50 years (mean 28 years)
Fenoproflic acid plain 600 mg daily (n=16)
Fenoproflic acid enteric coated 600 mg daily (n=16)
Baseline faecal blood loss 0.2 mL/day
Average daily blood loss over second week of treatment:
Fenoproflic acid plain 1.7 (±0.9 SD) mL/day
Fenoproflic acid enteric coated 1.1 (±1.1) mL/day
Values at one week similar to those at two weeks
No patient had blood loss greater than 5 mL/day
Individual patient data available
<table>
<thead>
<tr>
<th>Study</th>
<th>Method</th>
<th>Baseline faecal blood loss</th>
<th>Treatment Duration</th>
<th>Treatment Details</th>
<th>Blood loss Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jallad et al. Am J Med Sci 1986 292:272-276</td>
<td>Cr51-labelled RBC to measure faecal erythrocyte excretion in controlled conditions over 28 days treatment</td>
<td>0.4-1.2 mL/day</td>
<td>28 days</td>
<td>Men with osteoarthritis aged 28 to 70 years (mean 57 years) Etodolac 600 mg daily (n=8)</td>
<td>Etodolac 600 mg 0.7 (±0.4 SD) mL/day Etodolac 1000 mg 0.4 (±0.2) mL/day Piroxicam 20 mg 3.7 (±3.2) mL/day</td>
</tr>
<tr>
<td>Bird et al. Curr Med Res Ther 1985 9:524-528</td>
<td>Cr51-labelled RBC to measure faecal erythrocyte excretion in controlled conditions over 28 days</td>
<td>0.35 mL/day</td>
<td>28 days</td>
<td>Healthy male volunteers aged over 40 years (mean 52 years) Tenoxicam 20 mg daily (n=6) Piroxicam 20 mg daily (n=6)</td>
<td>Tenoxicam 1.2 mL/day Piroxicam 1.0 mL/day</td>
</tr>
<tr>
<td>Hooper et al. Clin Pharm Ther 1985 38: 533-537</td>
<td>Cr51-labelled RBC to measure faecal erythrocyte excretion in controlled conditions over 28 days</td>
<td>0.3 mL/day</td>
<td>28 days</td>
<td>Healthy male volunteers aged 18-40 years (mean 24 years) Isoxicam 200 mg daily (n=8) Piroxicam 20 mg daily (n=6)</td>
<td>Isoxicam 1.0 mL/day (±0.2 SD) mL/day Piroxicam 0.9 mL/day (±0.2) mL/day</td>
</tr>
<tr>
<td>Salom et al. J Clin Pharmacol 1984 24:240-246</td>
<td>Cr51-labelled RBC to measure faecal erythrocyte excretion in controlled conditions over 14 days.</td>
<td>0.3-0.5 mL/day</td>
<td>14 days</td>
<td>Healthy male volunteers aged 18-47 years Etodolac 800 mg daily (n=11) Etodolac 1,200 mg daily (n=12) Ibuprofen 2,400 mg daily (n=12) Indomethacin 200 mg daily (n=9) Naproxen 700 mg daily (n=9)</td>
<td>Etodolac 0.5 mL/day Etodolac 0.6 mL/day Ibuprofen 1.6 mL/day Indomethacin 1.7 mL/day Naproxen 1.2 mL/day</td>
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</tbody>
</table>

2/6 on piroxicam had mean daily blood loss >5 mL

Individual patient data available

No patient had blood loss of more than 5 mL/day

Values in weeks 2-4 similar

Data from two patients with higher levels of faecal blood loss (maximum 3.9 and 14 mL/day) omitted from piroxicam, and one (4.4 mL/day) from isoxicam. Clear spikes in blood loss in these patients

Individual patient data available

No dispersion given
<table>
<thead>
<tr>
<th>Study</th>
<th>Methodology</th>
<th>Volunteers</th>
<th>Treatment A</th>
<th>Treatment B</th>
<th>Blood Loss A</th>
<th>Blood Loss B</th>
<th>Allocation</th>
<th>Blinding</th>
<th>Individual Data</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bird et al. J Clin Pharmacol 1984 24: 240-246</td>
<td>Cr51-labelled RBC to measure faecal erythrocyte excretion in controlled conditions over two 14-day crossover periods</td>
<td>Healthy volunteers aged over 35 years (mean age 50 years), 11 male, 1 female</td>
<td>Ro 21-5521 250 mg daily</td>
<td>Placebo</td>
<td>Baseline faecal blood loss 0.5 mL/day</td>
<td>Average daily blood loss over last 4 days of treatment: Ro 21-5521 2.9 mL/day Placebo 0.5 mL/day</td>
<td>No dispersion given</td>
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<tr>
<td>Robbins et al. Clin Ther 1984 6: 461-466</td>
<td>Cr51-labelled RBC to measure faecal erythrocyte excretion in controlled conditions over 7 days.</td>
<td>Healthy male volunteers aged 18-35 years</td>
<td>Uncoated aspirin 2,925 mg daily (n=9)</td>
<td>Enteric coated aspirin 2,950 mg daily (n=10)</td>
<td>Baseline faecal blood loss 0.3 mL/day</td>
<td>Average daily blood loss over last 4 days of treatment: Uncoated aspirin 4.3 (±1.7 SD) mL/day Enteric coated aspirin 1.5 (±0.6) mL/day</td>
<td>3/9 with uncoated aspirin had blood loss &gt;5</td>
<td>Individual patient data available</td>
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<tr>
<td>Rider. Pharmacotherapy 1983 3 (Suppl 1): 61S-64S</td>
<td>Cr51-labelled RBC to measure faecal erythrocyte excretion in controlled conditions over 14 days.</td>
<td>Healthy male volunteers</td>
<td>Diflusinal 1,000 mg daily (n=12)</td>
<td>Aspirin 4,000 mg daily (n=12)</td>
<td>Baseline faecal blood loss 1.0 mL/day</td>
<td>Average daily blood loss over last 7 days of treatment: Diflusinal 2.1 mL/day Aspirin 8.8 mL/day Placebo 1.6 mL/day</td>
<td>Does not say allocation was at random, but excellent description of blinding. Assumed to be acceptable</td>
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<tr>
<td>Ranlov et al. Scand J Rheumatol 1983 12: 280-284</td>
<td>Cr51-labelled RBC to measure faecal erythrocyte excretion in controlled conditions over 7 days.</td>
<td>Healthy male student volunteers</td>
<td>Aspirin 4,000 mg daily (n=10)</td>
<td>Ketoprofen 200 mg daily (n=10)</td>
<td>8/10 with aspirin had blood loss &gt;4 mL/day, 2 &gt;25 mL/day</td>
<td>Individual patient data available, but not accurate values</td>
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<tr>
<td>Study</td>
<td>Methodology</td>
<td>Participants</td>
<td>Faecal Blood Loss Baseline</td>
<td>Faecal Blood Loss Average 4 Days Treatment</td>
<td>Dispersion</td>
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<tr>
<td>Arnold &amp; Berger. Pharmacology 1983 27 (suppl 1): 14-22</td>
<td>Cr51-labelled RBC to measure faecal erythrocyte excretion in controlled conditions over two 7-day crossover periods</td>
<td>Healthy male volunteers aged 23-57 years (mean age 38 years, n=20)</td>
<td>0.4 mL/day</td>
<td>Aspirin 4.2 mL/day</td>
<td>No dispersion given</td>
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<tr>
<td>Green et al. Pharmacotherapy 1983 3: 65S-69S (duplicate)</td>
<td>Cr51-labelled RBC to measure faecal erythrocyte excretion in controlled conditions over 7 days.</td>
<td>Healthy male and female volunteers aged 21-40 years</td>
<td>0.5 mL/day</td>
<td>Aspirin 6.1 mL/day</td>
<td>No accurate dispersion given</td>
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<tr>
<td>Guercolini et al. Clinical Trials Journal 1983 20: 53-58</td>
<td>Cr51-labelled RBC to measure faecal erythrocyte excretion in controlled conditions over two 8-day crossover periods</td>
<td>Healthy young volunteers (n=12), 10 male, 2 female</td>
<td>0.48 mL/day</td>
<td>Indomethacin 0.58 mL/day</td>
<td>Individual patient data available</td>
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<tr>
<td>Bird et al. Curr Med Res Op 1983 8: 412-416</td>
<td>Cr51-labelled RBC to measure faecal erythrocyte excretion in controlled conditions over two 14-day crossover periods</td>
<td>Healthy volunteers aged 34-59, 6 male, 2 female</td>
<td>0.3 mL/day</td>
<td>Aspirin 3,600 mg daily</td>
<td>No dispersion given</td>
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<td>Reference</td>
<td>Methodology</td>
<td>Baseline faecal blood loss</td>
<td>Median daily blood loss over last 5 days of treatment</td>
<td>Average daily blood loss over last 3 days of treatment</td>
<td>Notes</td>
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<tr>
<td>Dirksen et al. Scand J Rheumatol 1982 11: 129-132</td>
<td>Cr51-labelled RBC to measure faecal erythrocyte excretion in controlled conditions over two 7-day crossover periods</td>
<td>0.5 mL/day</td>
<td>2.6 mL/day (aspirin time release)</td>
<td>8.8 mL/day (aspirin)</td>
<td>One patient (AS) had average daily blood loss of up to 77 mL/day and had low Hb level</td>
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<tr>
<td>Lussier et al. J Clin Pharmacol 1982 22: 173-178</td>
<td>Cr51-labelled RBC to measure faecal erythrocyte excretion in controlled conditions over 14 days.</td>
<td>0.6 mL/day</td>
<td>1.1 mL/day (placebo)</td>
<td>8.8 mL/day (aspirin)</td>
<td>No dispersion given</td>
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<tr>
<td>Gillberg et al. Scand J Rheumatol 1981 10: 342-346</td>
<td>Cr51-labelled RBC to measure faecal erythrocyte excretion in controlled conditions over two 7-day crossover periods</td>
<td>0.5 mL/day</td>
<td>6.0 mL/day (aspirin)</td>
<td>2.3 mL/day (oxaprozin)</td>
<td>Individual patient data available</td>
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<tr>
<td>Study</td>
<td>Methodology</td>
<td>Baseline faecal blood loss</td>
<td>Average daily blood loss over last 3 days of treatment</td>
<td>Other observations</td>
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<tr>
<td>Johnson. J Clin Pharmacol 1980 20: 401-405 (two trials)</td>
<td>Cr51-labelled RBC to measure faecal erythrocyte excretion in controlled conditions over 7 days.</td>
<td>Baseline faecal blood loss under 1.1 mL/day (average 0.8 mL/day)</td>
<td>8/16 on aspirin had daily blood loss &gt;5 mL/day, and 2/16 ≥10 mL/day</td>
<td>No dispersion given</td>
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<tr>
<td>R = 1 DB = 1 W = 1 QS = 3</td>
<td>Healthy male and female volunteers (17 men, 15 women)</td>
<td>Trial 1: Aspirin 6.9 mL/day</td>
<td>4/16 on zomepirac had daily blood loss &gt;5 mL/day, and 3/16 ≥10 mL/day</td>
<td>Individual patient data available</td>
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<td>Trial 1: Aspirin 3,900 mg daily (n=8) Zomepirac 300 mg daily (n=8)</td>
<td>Zomepirac 3.3 mL/day</td>
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<td>Trial 2: Aspirin 4,800 mg daily (n=8) Zomepirac 600 mg daily (n=8)</td>
<td>Zomepirac 9.5 mL/day</td>
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<tr>
<td>Chernish et al. Arthritis Rheum 1979 22: 376-383</td>
<td>Cr51-labelled RBC to measure faecal erythrocyte excretion in controlled conditions over two 7-day crossover periods (placebo between active treatments)</td>
<td>Baseline faecal blood loss not measured</td>
<td>Average daily blood loss over last 4 days of treatment:</td>
<td>Individual patient data available</td>
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<tr>
<td>R = 1 DB = 2 W = 1 QS = 4</td>
<td>Healthy male Volunteers age 23-60 years, mean 44 years (n=16)</td>
<td>Trial: Aspirin 5.0 (±2.2 SD) mL/day</td>
<td>8/16 on aspirin had daily blood loss &gt;5 mL/day</td>
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<td></td>
<td>Aspirin 3,900 mg daily</td>
<td>Fenoprofen 2.5 (±1.2) mL/day</td>
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<td></td>
<td>Fenoprofen 2,400 mg daily</td>
<td>Placebo 0.8 (±0.6) mL/day</td>
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<tr>
<td>Welch et al. Gastroenterol 1978 74: 459-463</td>
<td>Cr51-labelled RBC to measure faecal erythrocyte excretion in controlled conditions over two 28-day crossover periods</td>
<td>Median daily blood loss over last 4 days of treatment:</td>
<td>4/22 patients on aspirin + placebo had mean daily faecal blood loss &gt;5 mL/day, and 1/22 &gt;10 mL/day</td>
<td>Note randomisation to cimetidine, not aspirin</td>
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<tr>
<td>R = 1 DB = 0 W = 1 QS = 2</td>
<td>Patients (RA, OA) (n=22) taking at least 2,600 mg aspirin daily</td>
<td>Aspirin + placebo 4.1 (±0.7 SEM) mL/day</td>
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<td>Individual patient data available from graph</td>
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<td></td>
<td>Aspirin + placebo</td>
<td>Aspirin + cimetidine 2.2 (±0.3) mL/day</td>
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<td>Study</td>
<td>RBC Label</td>
<td>Study Details</td>
<td>Baseline faecal blood loss</td>
<td>Treatment Details</td>
<td>Results</td>
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<td>DeSchepper et al. Clin Pharmacol Ther 1978 23:669-676</td>
<td>Cr51-labelled RBC</td>
<td>to measure faecal erythrocyte excretion in controlled conditions over two 7-day periods with 7-day washout (Note parallel study, phase 1 data used)</td>
<td>Baseline faecal blood loss average 0.32 mL/day</td>
<td>Mean daily blood loss over last five days of treatment: Aspirin 6.9 mL/day Diffusinal 0.32 mL/day</td>
<td>1/5 on aspirin had average daily blood loss &gt;10 mL/day</td>
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<tr>
<td>Baltes. J Clin Pharm 1977 17: 120-124</td>
<td>Cr51-labelled RBC</td>
<td>to measure faecal erythrocyte excretion in controlled conditions over two 7-day crossover periods</td>
<td>Baseline faecal blood loss 0.5 mL/day</td>
<td>Median daily blood loss over last 3 days of treatment: Aspirin 1.6 (±1.2 SD) mL/day Nefopam 0.6 (±0.4) mL/day</td>
<td>No individual had ≥5 mL/day blood loss on treatment</td>
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<tr>
<td>Vakil et al. Curr Med Res Op 1977 5: 32-37</td>
<td>Cr51-labelled RBC</td>
<td>to measure faecal erythrocyte excretion in controlled conditions over 7 days</td>
<td>Baseline faecal blood loss under 1 mL/day (average 0.8 mL/day)</td>
<td>Average daily blood loss over last 4 days of treatment: Flurbiprofen 2.5 (±2.6 SD) mL/day Phenylbutazone 1.3 (±1.5) mL/day Aspirin 3.2 (±1.4) mL/day Placebo 0.7 (±0.4) mL/day</td>
<td>No individual had ≥5 mL/day blood loss on treatment</td>
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<tr>
<td>Loebl et al. JAMA 1977 237: 976-981</td>
<td>Cr51-labelled RBC</td>
<td>to measure faecal erythrocyte excretion in controlled conditions over two 7-day crossover periods separated by two weeks using paracetamol</td>
<td>Baseline faecal blood loss not reported</td>
<td>Average daily blood loss over last 4 days of treatment: Aspirin 5.0 mL/day Fenoprofen 2.2 mL/day Paracetamol washout 0.8 mL/day</td>
<td>5/11 patients had daily faecal blood loss &gt;5 mL/day on aspirin, and 2/11 &gt;10 mL/day 1/12 patients on fenoprofen had blood loss &gt;5 mL/day</td>
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- DB = 2
- W = 0
- QS = 2

- DB = 2
- W = 1
- QS = 5
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<tr>
<th>Study</th>
<th>Protocol</th>
<th>Subjects</th>
<th>Drug Doses</th>
<th>Blood Loss Baseline</th>
<th>Treatment Blood Loss Last Day</th>
<th>Treatment Blood Loss Over 7 Days</th>
<th>Faecal Blood Loss &gt;5 mL/day</th>
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<tbody>
<tr>
<td>Mintz &amp; Fraga. Curr Med Res Op 1976 4: 89-93</td>
<td>Cr51-labelled RBC to measure faecal erythrocyte excretion in controlled conditions over 14 days</td>
<td>Patients with RA, 2 male 18 female</td>
<td>Azapropazone 600 mg daily (n=10)</td>
<td>Average daily blood loss over last 7 days of treatment:</td>
<td>1/10 on azapropazone 600 mg had mean faecal blood loss &gt;5 mL/day</td>
<td>Individual patient data available</td>
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<tr>
<td>Cohen. Clin Pharm Ther 1976 20: 238-240</td>
<td>Cr51-labelled RBC to measure faecal erythrocyte excretion in controlled conditions over 14 days</td>
<td>Men aged 21-45 years (mean 28 years)</td>
<td>Sulindac 240 mg daily (n=10)</td>
<td>Baseline faecal blood loss 0.4 mL/day</td>
<td>1/10 on aspirin had daily faecal blood loss of &gt;5 mL/day</td>
<td>No dispersion given</td>
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<tr>
<td>Leonards &amp; Levy. Clin Pharm Ther 1973 14: 62-66</td>
<td>Cr51-labelled RBC to measure faecal erythrocyte excretion in controlled conditions over two 7-day periods with washout</td>
<td>Healthy volunteers, 5 male 8 female, mean age 23 years</td>
<td>Aspirin 3,900 mg daily</td>
<td>Average daily blood loss over 7 days of treatment:</td>
<td>5/13 had daily faecal blood loss &gt;5 mL/day on aspirin, and 2/13 &gt;10 mL/day</td>
<td>Individual patient data available</td>
<td></td>
</tr>
<tr>
<td>Leonards &amp; Levy. Arch Intern Med 1972 129: 457-460</td>
<td>Cr51-labelled RBC to measure faecal erythrocyte excretion in controlled conditions over four 7-day periods with washout</td>
<td>Healthy volunteers, 7 male 8 female, mean age 26 years</td>
<td>Four different types of aspirin formulation, each at 2,600 mg daily</td>
<td>Baseline faecal blood loss 0.4 mL/day</td>
<td>1/15 had daily faecal blood loss &gt;5 mL/day on aspirin</td>
<td>Only preparation D was commercially available</td>
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<td>Average daily blood loss over 7 days of treatment:</td>
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<td>Individual patient data available</td>
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<td>Study</td>
<td>Medication</td>
<td>Study Design</td>
<td>Baseline Faecal Blood Loss</td>
<td>Average Daily Blood Loss Over 7 Days of Treatment</td>
<td>Faecal Blood Loss &gt;10 mL/day</td>
<td>Individual Patient Data Available</td>
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<tr>
<td>Leonards. J Lab Clin Med 1969 74: 911-914</td>
<td>Cr51-labelled RBC to measure faecal erythrocyte excretion in controlled conditions over four 7-day periods with washout</td>
<td>2/12 had daily faecal blood loss &gt;10 mL/day on aspirin</td>
<td>2/12 had daily faecal blood loss &gt;10 mL/day on aspirin</td>
<td>Healthy volunteers, 11 male 1 female, age 19-33 years</td>
<td>Aspirin 4.8 (±5.5 SD) mL/day</td>
<td>Individual patient data available</td>
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<tr>
<td>Rider et al. Clin Ther Res 1965 7: 633-638</td>
<td>Cr51-labelled RBC to measure faecal erythrocyte excretion in controlled conditions over 14 days</td>
<td>3/8 on aspirin had daily faecal blood loss of &gt;5 mL/day</td>
<td>3/8 on aspirin had daily faecal blood loss of &gt;5 mL/day</td>
<td>Normal volunteers in good health</td>
<td>Aspirin 4.0 (±1.0 SEM) mL/day</td>
<td>Individual patient data available</td>
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Abbreviations: R = randomised; SB = double blind; W = withdrawals and dropouts; QS = quality score; SD = standard deviations; OA = osteoarthritis; RA = rheumatoid arthritis; AS = ankylosing spondilitis