## **Supplemental material**

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| Table S1.  | Meta-regression analyses for TC, HDL-C, TG and LDL-C.                    |  |  |

Figure S1. PRISMA Flow Diagram

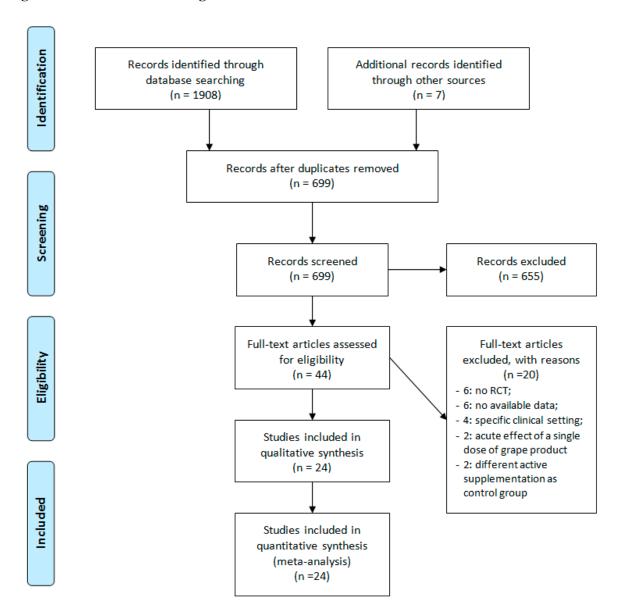


Figure S2. Changes in TC levels after administration of grape products as compared with controls

| Study name             | Sta                    | tistics for    | each study     | <u>y</u> |              | Difference       | in means a | nd 95% CI |
|------------------------|------------------------|----------------|----------------|----------|--------------|------------------|------------|-----------|
|                        | Difference<br>in means | Lower<br>limit | Upper<br>limit | p-Value  |              |                  |            |           |
| Argani 2016            | -25,000                | -28,462        | -21,538        | 0,000    | <del>-</del> | - I              | 1          | 1         |
| Banini 2006            | -4,800                 | -10,428        | 0,828          | 0,095    |              | l —              | ▆┤         |           |
| Dohadwala 2010         | -2,000                 | -4,533         | 0,533          | 0,122    |              |                  | -■         |           |
| Hansen 2005            | -8,500                 | -28,244        | 11,244         | 0,399    | —            | <del>-   -</del> | _          | <b>—</b>  |
| Hollis 2009            | -15,000                | -17,531        | -12,469        | 0,000    |              | -                |            |           |
| Jiménez 2008           | -19,100                | -28,146        | -10,054        | 0,000    | 1—           | -■-              |            |           |
| Kar 2009               | -4,000                 | -6,567         | -1,433         | 0,002    |              |                  | ╼╴         |           |
| Martinez-Maqueda 2018  | -4,000                 | -5,731         | -2,269         | 0,000    |              |                  |            |           |
| Mellen 2010            | -1,300                 | -3,650         | 1,050          | 0,278    |              |                  | -          |           |
| Millar 2018            | -11,000                | -16,205        | -5,795         | 0,000    |              | <del>  ■</del>   | -          |           |
| Park 2009              | -1,300                 | -8,037         | 5,437          | 0,705    |              | -                | ━          |           |
| Preuss 2000            | -3,000                 | -12,511        | 6,511          | 0,536    |              | I —              | ╼┼─        |           |
| Sano 2007              | 0,000                  | -5,235         | 5,235          | 1,000    |              |                  | -          |           |
| Siasos 2013            | -4,000                 | -12,188        | 4,188          | 0,338    |              | <del></del>      | -          |           |
| Sivaprakasapillai 2009 | -4,000                 | -6,741         | -1,259         | 0,004    |              |                  | ╼┈│        |           |
| Taghizadeh 2016        | -4,000                 | -7,434         | -0,566         | 0,022    |              | -                | -■-        |           |
| Tomé-Carneiro 2012     | -10,900                | -16,180        | -5,620         | 0,000    |              | <del>  ■</del>   | -          |           |
| Vaisman 2015           | -4,500                 | -7,736         | -1,264         | 0,006    |              | -                | ╼┈│        |           |
| Vigna 2003             | -8,000                 | -11,038        | -4,962         | 0,000    |              | -■               | -          |           |
| Yubero 2013            | -25,800                | -28,954        | -22,646        | 0,000    | -            |                  |            |           |
| Zem 2005 (a)           | -4,000                 | -7,405         | -0,595         | 0,021    |              | .                | ╼┈│        |           |
| Zem 2005 (b)           | -4,000                 | -8,493         | 0,493          | 0,081    |              | -                | ╼┤         |           |
|                        | -7,625                 | -10,832        | -4,419         | 0,000    |              |                  | <b>-</b>   |           |
|                        |                        |                |                |          | -30,00       | -15,00           | 0,00       | 15,00     |

Figure S3. Changes in HDL-C levels after administration of grape products as compared with controls.

| Study name             | Statistics for each study |                |                |         | Difference | in means a | nd 95% CI       |       |
|------------------------|---------------------------|----------------|----------------|---------|------------|------------|-----------------|-------|
|                        | Difference<br>in means    | Lower<br>limit | Upper<br>limit | p-Value |            |            |                 |       |
| Argani 2016            | 7,300                     | -12,995        | 27,595         | 0,481   | ſ          | 1-         | <del></del>     | -     |
| Banini 2006            | 0,700                     | -1,975         | 3,375          | 0,608   |            |            | -               |       |
| Dohadwala 2010         | 1,000                     | -0,326         | 2,326          | 0,140   |            |            | -               |       |
| Hansen 2005            | 1,500                     | -5,929         | 8,929          | 0,692   |            |            | -               | -     |
| Hollis 2009            | 2,000                     | 0,961          | 3,039          | 0,000   |            | l          |                 |       |
| Jiménez 2008           | 2,500                     | 0,786          | 4,214          | 0,004   |            |            | -               |       |
| Kar 2009               | 0,000                     | -0,854         | 0,854          | 1,000   |            |            | •               |       |
| Martinez-Maqueda 2018  | 2,000                     | -1,315         | 5,315          | 0,237   |            | l          | <del> ■</del> - |       |
| Mellen 2010            | 0,700                     | 0,126          | 1,274          | 0,017   |            | l          |                 |       |
| Millar 2018            | 0,900                     | -1,264         | 3,064          | 0,415   |            |            | -               |       |
| Park 2009              | 2,000                     | 1,271          | 2,729          | 0,000   |            |            |                 |       |
| Preuss 2000            | 1,600                     | -1,062         | 4,262          | 0,239   |            |            | +=-             |       |
| Sano 2007              | 0,200                     | -1,461         | 1,861          | 0,813   |            |            |                 |       |
| Sivaprakasapillai 2009 | 3,000                     | 2,255          | 3,745          | 0,000   |            |            |                 |       |
| Taghizadeh 2016        | 4,000                     | 2,218          | 5,782          | 0,000   |            |            |                 |       |
| Tomé-Carneiro 2012     | 1,500                     | 0,415          | 2,585          | 0,007   |            |            |                 |       |
| Urquiaga 2015          | 1,900                     | -0,578         | 4,378          | 0,133   |            |            | =               |       |
| Vaisman 2015           | 0,900                     | -0,907         | 2,707          | 0,329   |            |            | -               |       |
| Vigna 2003             | 0,100                     | -0,848         | 1,048          | 0,836   |            | I          |                 |       |
| Yubero 2013            | 2,500                     | 1,870          | 3,130          | 0,000   |            |            |                 |       |
| Zem 2005 (a)           | 0,000                     | -0,805         | 0,805          | 1,000   |            |            | •               |       |
| Zem 2005 (b)           | 0,000                     | -1,260         | 1,260          | 1,000   |            |            | •               |       |
| Zunino 2014            | 2,170                     | 0,224          | 4,116          | 0,029   |            |            | -               |       |
|                        | 1,371                     | 0,840          | 1,902          | 0,000   |            | ı          | •               |       |
|                        |                           |                |                |         | -30,00     | -15,00     | 0,00            | 15,00 |

Figure S4. Changes in TG levels after administration of grape products as compared with controls

| Study name             | Stat                   | tistics for    | each stud      | <u>y</u> |        | Difference |          | in means a      |
|------------------------|------------------------|----------------|----------------|----------|--------|------------|----------|-----------------|
|                        | Difference<br>in means | Lower<br>limit | Upper<br>limit | p-Value  |        |            |          |                 |
| Argani 2016            | -30,700                | -34,957        | -26,443        | 0,000    | - 1    | +          |          |                 |
| Banini 2006            | -6,000                 | -16,575        | 4,575          | 0,266    |        | .          |          | <del>-</del> ■+ |
| Dohadwala 2010         | -7,000                 | -15,522        | 1,522          | 0,107    |        |            | -        | -■-             |
| Hansen 2005            | -2,600                 | -19,094        | 13,894         | 0,757    |        | -          | _        | -               |
| Hollis 2009            | -6,000                 | -21,494        | 9,494          | 0,448    |        | -          | _        |                 |
| Jiménez 2008           | -19,900                | -34,253        | -5,547         | 0,007    |        | -          |          | -               |
| Kar 2009               | -26,900                | -34,174        | -19,626        | 0,000    |        |            |          |                 |
| Martinez-Maqueda 2018  | -9,000                 | -10,195        | -7,805         | 0,000    |        |            |          |                 |
| Mellen 2010            | -6,800                 | -7,227         | -6,373         | 0,000    |        |            |          |                 |
| Millar 2018            | -49,000                | -58,481        | -39,519        | 0,000    |        | -          |          |                 |
| Park 2009              | -1,700                 | -39,292        | 35,892         | 0,929    |        | -          |          | =               |
| Sano 2007              | -13,000                | -20,207        | -5,793         | 0,000    |        |            |          | .               |
| Sivaprakasapillai 2009 | -6,000                 | -9,356         | -2,644         | 0,000    |        |            | 1        | <b>ĕ</b>        |
| Taghizadeh 2016        | -18,000                | -20,367        | -15,633        | 0,000    |        |            | 1        |                 |
| Tomé-Carneiro 2012     | -11,800                | -20,433        | -3,167         | 0,007    |        | -          |          | -               |
| Urquiaga 2015          | -27,400                | -39,451        | -15,349        | 0,000    |        | -          |          |                 |
| Vaisman 2015           | -6,200                 | -14,294        | 1,894          | 0,133    |        |            | -        | +               |
| Vigna 2003             | -18,000                | -29,297        | -6,703         | 0,002    |        | -          | $\vdash$ |                 |
| Zern 2005 (a)          | -17,700                | -24,131        | -11,269        | 0,000    |        | -          | H        |                 |
| Zern 2005 (b)          | -8,000                 | -18,961        | 2,961          | 0,153    |        | -          | -        | +               |
| Zunino 2014            | -0,600                 | -8,035         | 6,835          | 0,874    |        |            | $\dashv$ | <b>•</b> -      |
|                        | -14,475                | -17,778        | -11,172        | 0,000    | 1      |            | •        |                 |
|                        |                        |                |                |          | -60,00 | -30,00     | 0,       | 00              |

Figure S5. Funnel plots of effect size versus standard error for studies evaluating levels of TC (panel A), HDL-C (panel B), LDL-C (panel C) after administration of grape products or placebo.

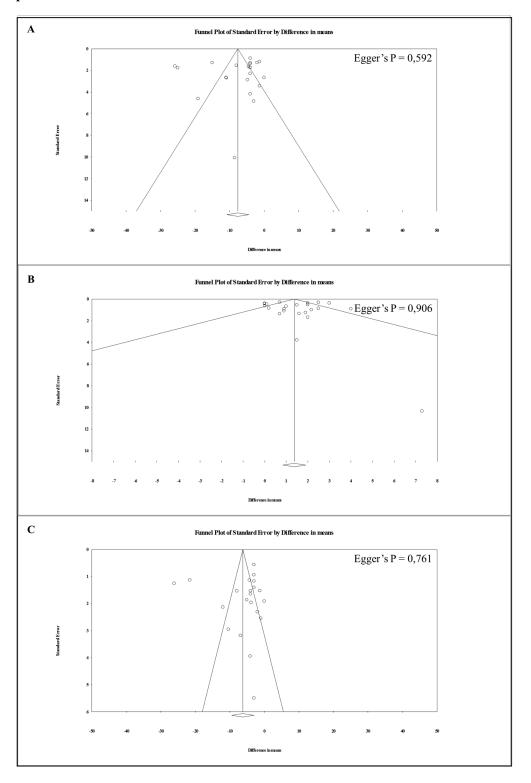


Figure S6. Funnel plots of effect size versus standard error (panel A) and Duval and Tweedie's trim and fill analysis (panel B) for studies evaluating levels of TG after administration of grape products or placebo.

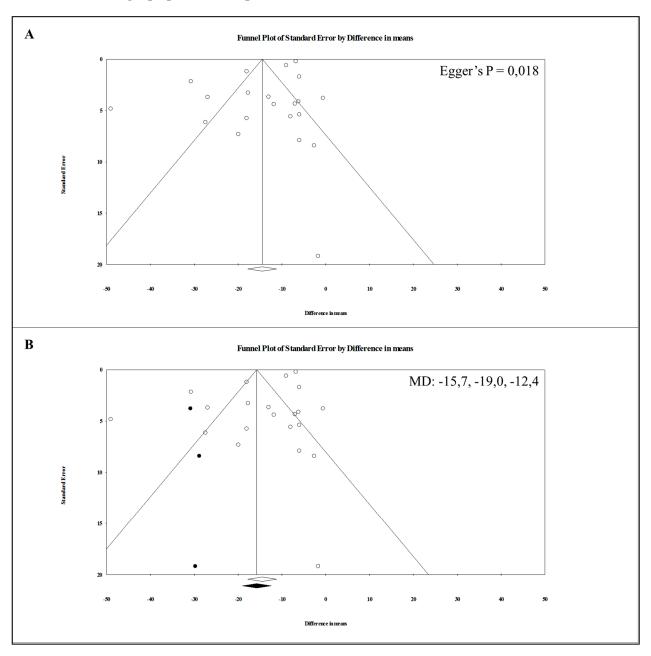


Table S1. Meta-regression analyses for TC, HDL-C, TG and LDL-C.

| A) TC (22 datasets -21 studies) | <b>Z</b> -value | P-value |
|---------------------------------|-----------------|---------|
| Age                             | 0.29            | 0.77    |
| Male gender                     | 0.34            | 0.73    |
| BMI                             | 0.34            | 0.74    |
| Diabetes                        | 0.63            | 0.53    |
| Dyslipidemia                    | 0.19            | 0.85    |
| Follow up                       | -1.33           | 0.19    |

| B) HDL-C (23 datasets – 22 studies) | Z-value | P-value |
|-------------------------------------|---------|---------|
| Age                                 | -2.58   | 0.01    |
| Male gender                         | -0.19   | 0.85    |
| BMI                                 | -0.34   | 0.74    |
| Diabetes                            | -1.54   | 0.12    |
| Dyslipidemia                        | -0.51   | 0.61    |
| Follow up                           | 1.02    | 0.31    |

| C) TG (21 datasets – 20 studies) | Z-value | P-value |
|----------------------------------|---------|---------|
| Age                              | -0.59   | 0.56    |
| Male gender                      | -0.34   | 0.73    |
| BMI                              | 0.82    | 0.41    |
| Diabetes                         | -1.25   | 0.21    |
| Dyslipidemia                     | -1.86   | 0.06    |
| Follow up                        | -0,29   | 0.77    |

| D) LDL-C (21 datasets – 20 studies) | <b>Z</b> -value | P-value |
|-------------------------------------|-----------------|---------|
| Age                                 | -0.19           | 0.84    |
| Male gender                         | 0.97            | 0.33    |
| BMI                                 | -0.24           | 0.81    |
| Diabetes                            | 0.72            | 0.47    |
| Dyslipidemia                        | -0.13           | 0.90    |
| Follow up                           | 0.23            | 0.82    |