

```

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<?mso-application progid="Word.Document"?>
<pkg:package xmlns:pkg="http://schemas.microsoft.com/office/2006/xmlPackage">
  - <pkg:part pkg:padding="512" pkg:contentType="application/vnd.openxmlformats-package.relationships+xml" pkg:name="/_rels/.rels">
    - <pkg:xmlData>
      - <Relationships xmlns="http://schemas.openxmlformats.org/package/2006/relationships">
        <Relationship Target="docProps/app.xml" Type="http://schemas.openxmlformats.org/officeDocument/2006/relationships/extended-properties"
          Id="rId3"/>
        <Relationship Target="docProps/core.xml" Type="http://schemas.openxmlformats.org/package/2006/relationships/metadata/core-properties"
          Id="rId2"/>
        <Relationship Target="word/document.xml" Type="http://schemas.openxmlformats.org/officeDocument/2006/relationships/officeDocument"
          Id="rId1"/>
      </Relationships>
    </pkg:xmlData>
  </pkg:part>
  - <pkg:part pkg:contentType="application/vnd.openxmlformats-officedocument.wordprocessingml.document.main+xml" pkg:name="/word/document.xml">
    - <pkg:xmlData>
      - <w:document mc:Ignorable="w14 w15 w16se w16cid wp14" xmlns:wps="http://schemas.microsoft.com/office/word/2010/wordprocessingShape"
        xmlns:wne="http://schemas.microsoft.com/office/word/2006/wordml" xmlns:wpi="http://schemas.microsoft.com/office/word/2010/wordprocessingInk"
        xmlns:wpg="http://schemas.microsoft.com/office/word/2010/wordprocessingGroup"
        xmlns:w16se="http://schemas.microsoft.com/office/word/2015/wordml/symex"
        xmlns:w16cid="http://schemas.microsoft.com/office/word/2016/wordml/cid" xmlns:w15="http://schemas.microsoft.com/office/word/2012/wordml"
        xmlns:w14="http://schemas.microsoft.com/office/word/2010/wordml" xmlns:w="http://schemas.openxmlformats.org/wordprocessingml/2006/main"
        xmlns:w10="urn:schemas-microsoft-com:office:word" xmlns:wp="http://schemas.openxmlformats.org/drawingml/2006/wordprocessingDrawing"
        xmlns:wp14="http://schemas.microsoft.com/office/word/2010/wordprocessingDrawing" xmlns:v="urn:schemas-microsoft-com:vml"
        xmlns:m="http://schemas.openxmlformats.org/officeDocument/2006/math"
        xmlns:r="http://schemas.openxmlformats.org/officeDocument/2006/relationships" xmlns:o="urn:schemas-microsoft-com:office:office"
        xmlns:am3d="http://schemas.microsoft.com/office/drawing/2017/model3d" xmlns:aink="http://schemas.microsoft.com/office/drawing/2016/ink"
        xmlns:mc="http://schemas.openxmlformats.org/markup-compatibility/2006"
        xmlns:cx8="http://schemas.microsoft.com/office/drawing/2016/5/14/chartex"
        xmlns:cx7="http://schemas.microsoft.com/office/drawing/2016/5/13/chartex"
        xmlns:cx6="http://schemas.microsoft.com/office/drawing/2016/5/12/chartex"
        xmlns:cx5="http://schemas.microsoft.com/office/drawing/2016/5/11/chartex"
        xmlns:cx4="http://schemas.microsoft.com/office/drawing/2016/5/10/chartex"
        xmlns:cx3="http://schemas.microsoft.com/office/drawing/2016/5/9/chartex"
        xmlns:cx2="http://schemas.microsoft.com/office/drawing/2015/10/21/chartex"
        xmlns:cx1="http://schemas.microsoft.com/office/drawing/2015/9/8/chartex" xmlns:cx="http://schemas.microsoft.com/office/drawing/2014/chartex"
        xmlns:wpc="http://schemas.microsoft.com/office/word/2010/wordprocessingCanvas">
        - <w:body>
          - <w:p w:rsidP="00C62C26" w:rsidRDefault="00C62C26" w:rsidR="00C62C26" w14:textId="77777777" w14:paraId="01CF1B10">
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              <w:jc w:val="left"/>
            - <w:rPr>
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              <w:color w:val="385623" w:themeShade="80" w:themeColor="accent6"/>
              <w:sz w:val="16"/>
              <w:szCs w:val="16"/>
            </w:rPr>
          </w:pPr>
          <w:bookmarkStart w:name="_GoBack" w:id="0"/>
          <w:bookmarkEnd w:id="0"/>
          - <w:r w:rsidRPr="005C028C">
            - <w:rPr>
              <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI Semilight"/>
              <w:color w:val="385623" w:themeShade="80" w:themeColor="accent6"/>
              <w:sz w:val="16"/>
              <w:szCs w:val="16"/>
            </w:rPr>
            <w:t>The North African Journal of Fo</w:t>
          </w:r>
        - <w:r>
          - <w:rPr>
            <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI Semilight"/>
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            <w:sz w:val="16"/>
            <w:szCs w:val="16"/>
          </w:rPr>
          <w:t>od and Nu</w:t>
        </w:r>
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          </w:rPr>
          <w:t>trition Research: (2019) 03; (05</w:t>
        </w:r>
        - <w:r w:rsidR="00ED4AB9">
          - <w:rPr>

```

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- <w:r w:rsidR="00B94ADB">
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        <w:szCs w:val="16"/>
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</w:pPr>
- <w:r>
    - <w:rPr>
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relativeHeight="251707392" simplePos="0" distR="114300" distL="114300" distB="0" distT="0">
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        </wp:positionH>
        - <wp:positionV relativeFrom="paragraph">
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        </wp:positionV>
        <wp:extent cx="948985" cy="385156"/>
        <wp:effectExtent r="3810" b="0" t="0" l="0"/>
        <wp:wrapNone/>
        <wp:docPr name="Picture 33" id="33" descr="Image result for open access logo"/>
    - <wp:cNvGraphicFramePr>
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    </wp:cNvGraphicFramePr>
    - <a:graphic xmlns:a="http://schemas.openxmlformats.org/drawingml/2006/main">
        - <a:graphicData uri="http://schemas.openxmlformats.org/drawingml/2006/picture">
            - <pic:pic xmlns:pic="http://schemas.openxmlformats.org/drawingml/2006/picture">
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                    <pic:cNvPr name="Picture 1" id="0" descr="Image result for open access logo"/>
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            - <pic:blipFill>

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- <a:blip cstate="print" r:embed="rId8">
  - <a:extLst>
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    </a:ext>
  </a:extLst>
</a:blip>
<a:srcRect/>
- <a:stretch>
  <a:fillRect/>
</a:stretch>
</pic:blipFill>
- <pic:spPr bwMode="auto">
  - <a:xfrm>
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  </a:xfrm>
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  </a:prstGeom>
  <a:noFill/>
  - <a:ln>
    <a:noFill/>
  </a:ln>
</pic:spPr>
</pic:pic>
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</a:graphic>
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- <wp14:sizeRelV relativeFrom="margin">
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</w:r>
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    - <w:rPr>
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      <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI Semilight"
        w:eastAsia="Leelawadee UI Semilight"/>
      <w:sz w:val="16"/>
      <w:lang w:val="fr-FR"/>
    </w:rPr>
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  </w:r>
  - <w:r w:rsidR="007A215C" w:rsidRPr="007A215C">
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</w:p>
- <w:p w:rsidP="008B0DCA" w:rsidRDefault="005B7D45" w:rsidR="00C62C26" w14:textId="77777777" w14:paraId="27369524"
  w:rsidRPr="00ED042C">
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  - <w:rPr>
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- <w:r w:rsidRPr="00ED042C">
  - <w:rPr>
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[illegible]

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        <w:tab/>
    </w:r>
</w:p>
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    - <w:rPr>
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                        - <wps:style>
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- <mc:Fallback>
- <w:pict>
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distance-left:9pt;mso-wrap-distance-top:0;mso-wrap-distance-right:9pt;mso-wrap-distance-bottom:0;mso-position-
horizontal:absolute;mso-position-horizontal-relative:page;mso-position-vertical:bottom;mso-position-vertical-
relative:bottom;text-align:center" o:spid="_x0000_s1026">
<v:stroke joinstyle="miter" miterlimit="83231f"/>
<v:path textbboxrect="0,0,5981426,12192" arrowok="t"/>
<w:wrap anchortype="page"/>
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- <wp:positionV relativeFrom="paragraph">
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- <a:graphic xmlns:a="http://schemas.openxmlformats.org/drawingml/2006/main">
- <a:graphicData uri="http://schemas.microsoft.com/office/word/2010/wordprocessingShape">
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- <a:pathLst>
  - <a:path w="5981426" h="12192">
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```

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        - <a:graphic xmlns:a="http://schemas.openxmlformats.org/drawingml/2006/main">
          - <a:graphicData uri="http://schemas.microsoft.com/office/word/2010/wordprocessingShape">
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                </a:prstGeom>
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    </w:rPr>
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  <w:proofErr w:type="spellEnd"/>
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</w:p>
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- <mc:Fallback>
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```

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percent:0;mso-height-percent:0;mso-width-relative:margin;mso-height-relative:margin;v-text-anchor:top"
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            <w:ind w:left="11" w:hanging="11"/>
            <w:jc w:val="right"/>
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            <w:b/>
            <w:bCs/>
            <w:color w:val="538135" w:themeShade="BF" w:themeColor="accent6"/>
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        </w:pPr>
        <w:proofErr w:type="spellStart"/>
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        - <w:rPr>
          <w:b/>
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        <w:t>eISSN</w:t>
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        <w:b/>
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  </w:p>
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              NAJFNR\Website\Images\NAJFNR Logo.png"/>
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    - <a:blip cstate="print" r:embed="rId10">
      - <a:extLst>
        - <a:ext uri="{28A0092B-C50C-407E-A947-70E740481C1C}">
          <a14:useLocalDpi val="0"
            xmlns:a14="http://schemas.microsoft.com/office/drawing/2010/main"/>
        </a:ext>
      </a:extLst>
    </a:blip>
    <a:srcRect/>
  - <a:stretch>
    <a:fillRect/>
  </a:stretch>
</pic:blipFill>
- <pic:spPr bwMode="auto">
  - <a:xfrm>
    <a:off y="0" x="0"/>
    <a:ext cx="1442720" cy="951230"/>
  </a:xfrm>
  - <a:prstGeom prst="rect">
    <a:avLst/>
  </a:prstGeom>
  <a:noFill/>
  - <a:ln>
    <a:noFill/>
  </a:ln>
</pic:spPr>
</pic:pic>
<a:graphicData>
  <a:graphic>
    - <wp14:sizeRelH relativeFrom="margin">
      <wp14:pctWidth>0</wp14:pctWidth>
    </wp14:sizeRelH>
    - <wp14:sizeRelV relativeFrom="margin">
      <wp14:pctHeight>0</wp14:pctHeight>
    </wp14:sizeRelV>
  </wp:anchor>
</w:drawing>
</w:r>
- <w:r w:rsidR="00C62C26" w:rsidPr="005C028C">
  - <w:rPr>
    <w:noProof/>
    <w:sz w:val="22"/>
  </w:rPr>
  - <mc:AlternateContent>
    - <mc:Choice Requires="wpg">
      - <w:drawing>
        - <wp:inline wp14:editId="5F472082" wp14:anchorId="089BE259" distR="0" distL="0" distB="0" distT="0">
          <wp:extent cx="5988055" cy="1014412"/>
          <wp:effectExtent r="0" b="0" t="0" l="0"/>
          <wp:docPr name="Group 10991" id="10991"/>
          <wp:cNvGraphicFramePr>
            - <a:graphic xmlns:a="http://schemas.openxmlformats.org/drawingml/2006/main">
              - <a:graphicData uri="http://schemas.microsoft.com/office/word/2010/wordprocessingGroup">
                - <wpg:wpg>
                  <wpg:cNvGrpSpPr>
                    - <wpg:grpSpPr>
                      - <a:xfrm>
                        <a:off y="0" x="0"/>
                        <a:ext cx="5988055" cy="1014412"/>
                        <a:chOff y="39628" x="-43766"/>
                        <a:chExt cx="5988055" cy="1122214"/>
                      </a:xfrm>
                    </wpg:grpSpPr>
                  - <wps:wsp>
                    <wps:cNvPr name="Rectangle 147" id="147">
                      <wps:cNvSpPr/>
                    - <wps:spPr>
                      - <a:xfrm>
                        <a:off y="39628" x="2990669"/>
                        <a:ext cx="42144" cy="186477"/>
                      </a:xfrm>
                      - <a:prstGeom prst="rect">
                        <a:avLst/>
                      </a:prstGeom>
                      - <a:ln>
                        <a:noFill/>
                      </a:ln>
                    </wps:spPr>
                  </wps:wsp>
                </wpg:wpg>
              </a:graphicData>
            </a:graphic>
          </wp:cNvGraphicFramePr>
        </wp:inline>
      </w:drawing>
    </mc:Choice>
  </mc:AlternateContent>
</w:r>

```

```

- <wps:txbx>
  - <w:txbxContent>
    - <w:p w:rsidP="00C62C26" w:rsidRDefault="00F806F5" w:rsidR="00F806F5"
      w14:textId="77777777" w14:paraId="135A0000">
        - <w:pPr>
          <w:spacing w:lineRule="auto" w:line="259" w:after="160" w:before="0"/>
          <w:ind w:right="0" w:left="0" w:firstLine="0"/>
          <w:jc w:val="left"/>
        </w:pPr>
        - <w:r>
          - <w:rPr>
            <w:sz w:val="22"/>
          </w:rPr>
          <w:t xml:space="preserve"></w:t>
        </w:r>
      </w:p>
    </w:txbxContent>
  </wps:txbx>
  - <wps:bodyPr bIns="0" rIns="0" tIns="0" lIns="0" vert="horz" rtlCol="0"
    horzOverflow="overflow">
    <a:noAutofit/>
  </wps:bodyPr>
</wps:wsp>
- <wps:wsp>
  <wps:cNvPr name="Rectangle 148" id="148"/>
  <wps:cNvSpPr/>
  - <wps:spPr>
    - <a:xfrm>
      <a:off y="507496" x="2990669"/>
      <a:ext cx="42144" cy="186477"/>
    </a:xfrm>
    - <a:prstGeom prst="rect">
      <a:avLst/>
    </a:prstGeom>
    - <a:ln>
      <a:noFill/>
    </a:ln>
  </wps:spPr>
- <wps:txbx>
  - <w:txbxContent>
    - <w:p w:rsidP="00C62C26" w:rsidRDefault="00F806F5" w:rsidR="00F806F5"
      w14:textId="77777777" w14:paraId="782B5C22">
        - <w:pPr>
          <w:spacing w:lineRule="auto" w:line="259" w:after="160" w:before="0"/>
          <w:ind w:right="0" w:left="0" w:firstLine="0"/>
          <w:jc w:val="left"/>
        </w:pPr>
        - <w:r>
          - <w:rPr>
            <w:sz w:val="22"/>
          </w:rPr>
          <w:t xml:space="preserve"></w:t>
        </w:r>
      </w:p>
    </w:txbxContent>
  </wps:txbx>
  - <wps:bodyPr bIns="0" rIns="0" tIns="0" lIns="0" vert="horz" rtlCol="0"
    horzOverflow="overflow">
    <a:noAutofit/>
  </wps:bodyPr>
</wps:wsp>
- <wps:wsp>
  <wps:cNvPr name="Rectangle 149" id="149"/>
  <wps:cNvSpPr/>
  - <wps:spPr>
    - <a:xfrm>
      <a:off y="975365" x="2990669"/>
      <a:ext cx="42144" cy="186477"/>
    </a:xfrm>
    - <a:prstGeom prst="rect">
      <a:avLst/>
    </a:prstGeom>
    - <a:ln>
      <a:noFill/>
    </a:ln>
  </wps:spPr>
- <wps:txbx>
  - <w:txbxContent>
    - <w:p w:rsidP="00C62C26" w:rsidRDefault="00F806F5" w:rsidR="00F806F5"
      w14:textId="77777777" w14:paraId="1DA436B8">
        - <w:pPr>
          <w:spacing w:lineRule="auto" w:line="259" w:after="160" w:before="0"/>

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        <w:ind w:right="0" w:left="0" w:firstLine="0"/>
        <w:jc w:val="left"/>
      </w:pPr>
    - <w:r>
      - <w:rPr>
        <w:sz w:val="22"/>
      </w:rPr>
      <w:t xml:space="preserve"></w:t>
    </w:r>
  </w:p>
</w:txbxContent>
</wps:txbx>
- <wps:bodyPr bIns="0" rIns="0" tIns="0" lIns="0" vert="horz" rtlCol="0"
  horzOverflow="overflow">
  <a:noAutofit/>
</wps:bodyPr>
</wps:wsp>
- <wps:wsp>
  <wps:cNvPr name="Rectangle 239" id="239"/>
  <wps:cNvSpPr/>
  - <wps:spPr>
    - <a:xfrm>
      <a:off y="517241" x="1971991"/>
      <a:ext cx="1781790" cy="168235"/>
    </a:xfrm>
    - <a:prstGeom prst="rect">
      <a:avLst/>
    </a:prstGeom>
    - <a:ln>
      <a:noFill/>
    </a:ln>
  </wps:spPr>
- <wps:txbx>
  - <w:txbxContent>
    - <w:p w:rsidP="00C62C26" w:rsidRDefault="00F806F5" w:rsidR="00F806F5"
      w14:textId="77777777" w14:paraId="420CEB61" w:rsidRP="00B409E3">
      - <w:pPr>
        <w:spacing w:lineRule="auto" w:line="259" w:after="160" w:before="0"/>
        <w:ind w:right="0" w:left="0" w:firstLine="0"/>
        <w:jc w:val="center"/>
      - <w:rPr>
        <w:rFonts w:hAnsi="Tw Cen MT" w:ascii="Tw Cen MT"/>
      </w:rPr>
    </w:pPr>
    - <w:r w:rsidRP="00B409E3">
      - <w:rPr>
        <w:rFonts w:hAnsi="Tw Cen MT" w:ascii="Tw Cen MT"/>
      </w:rPr>
      <w:t>Contents lists available at</w:t>
    </w:r>
  </w:p>
</w:txbxContent>
</wps:txbx>
- <wps:bodyPr bIns="0" rIns="0" tIns="0" lIns="0" vert="horz" rtlCol="0"
  horzOverflow="overflow">
  <a:noAutofit/>
</wps:bodyPr>
</wps:wsp>
- <wps:wsp>
  <wps:cNvPr name="Rectangle 242" id="242"/>
  <wps:cNvSpPr/>
  - <wps:spPr>
    - <a:xfrm>
      <a:off y="555884" x="3543881"/>
      <a:ext cx="38021" cy="168235"/>
    </a:xfrm>
    - <a:prstGeom prst="rect">
      <a:avLst/>
    </a:prstGeom>
    - <a:ln>
      <a:noFill/>
    </a:ln>
  </wps:spPr>
- <wps:txbx>
  - <w:txbxContent>
    - <w:p w:rsidP="00C62C26" w:rsidRDefault="00F806F5" w:rsidR="00F806F5"
      w14:textId="77777777" w14:paraId="3F7229C6">
      - <w:pPr>
        <w:spacing w:lineRule="auto" w:line="259" w:after="160" w:before="0"/>
        <w:ind w:right="0" w:left="0" w:firstLine="0"/>
        <w:jc w:val="left"/>
      </w:pPr>

```

```

- <w:r>
  <w:t xml:space="preserve"></w:t>
</w:r>
</w:p>
</w:txbxContent>
</wps:txbx>
- <wps:bodyPr bIns="0" rIns="0" tIns="0" lIns="0" vert="horz" rtlCol="0"
  horzOverflow="overflow">
  <a:noAutofit/>
</wps:bodyPr>
</wps:wsp>
- <wps:wsp>
  <wps:cNvPr name="Shape 13829" id="13829"/>
  <wps:cNvSpPr/>
  - <wps:spPr>
    - <a:xfrm>
      <a:off y="673229" x="-43766"/>
      <a:ext cx="5981064" cy="365760"/>
    </a:xfrm>
    - <a:custGeom>
      <a:avLst/>
      <a:gdLst/>
      <a:ahLst/>
      <a:cxnLst/>
      <a:rect r="0" b="0" t="0" l="0"/>
      - <a:pathLst>
        - <a:path w="5467472" h="365760">
          - <a:moveTo>
            <a:pt y="0" x="0"/>
          </a:moveTo>
          - <a:lnTo>
            <a:pt y="0" x="5467472"/>
          </a:lnTo>
          - <a:lnTo>
            <a:pt y="365760" x="5467472"/>
          </a:lnTo>
          - <a:lnTo>
            <a:pt y="365760" x="0"/>
          </a:lnTo>
          - <a:lnTo>
            <a:pt y="0" x="0"/>
          </a:lnTo>
        </a:path>
      </a:pathLst>
    </a:custGeom>
    - <a:solidFill>
      - <a:schemeClr val="accent6">
        <a:lumMod val="40000"/>
        <a:lumOff val="60000"/>
      </a:schemeClr>
    </a:solidFill>
    - <a:ln w="0" cap="rnd">
      <a:miter lim="127000"/>
    </a:ln>
  </wps:spPr>
- <wps:style>
  - <a:lnRef idx="0">
    - <a:srgbClr val="000000">
      <a:alpha val="0"/>
    </a:srgbClr>
  </a:lnRef>
  - <a:fillRef idx="1">
    <a:srgbClr val="F2F2F2"/>
  </a:fillRef>
  - <a:effectRef idx="0">
    <a:scrgbClr r="0" b="0" g="0"/>
  </a:effectRef>
  <a:fontRef idx="none"/>
</wps:style>
</wps:bodyPr>
</wps:wsp>
- <wps:wsp>
  <wps:cNvPr name="Rectangle 244" id="244"/>
  <wps:cNvSpPr/>
  - <wps:spPr>
    - <a:xfrm>
      <a:off y="697360" x="1835110"/>
      <a:ext cx="2933739" cy="168235"/>
    </a:xfrm>
    - <a:prstGeom prst="rect">
      <a:avLst/>
    </a:prstGeom>

```

```

- <a:ln>
  <a:noFill/>
</a:ln>
</wps:spPr>
- <wps:txbx>
  - <w:txbxContent>
    - <w:p w:rsidP="00C62C26" w:rsidRDefault="00F806F5" w:rsidR="00F806F5"
      w14:textId="77777777" w14:paraId="796177D0" w:rsidRPr="00B409E3">
      - <w:pPr>
        <w:spacing w:lineRule="auto" w:line="259" w:after="160" w:before="0"/>
        <w:ind w:right="0" w:left="0" w:firstLine="0"/>
        <w:jc w:val="left"/>
      - <w:rPr>
        <w:rFonts w:hAnsi="Tw Cen MT" w:ascii="Tw Cen MT"/>
      </w:rPr>
    </w:pPr>
    - <w:r w:rsidRPr="00B409E3">
      - <w:rPr>
        <w:rFonts w:hAnsi="Tw Cen MT" w:ascii="Tw Cen MT"/>
      </w:rPr>
      <w:t xml:space="preserve">Journal homepage: </w:t>
    </w:r>
    - <w:hyperlink rid="rId11" w:history="1">
      - <w:r w:rsidRPr="00B409E3">
        - <w:rPr>
          <w:rStyle w:val="Hyperlink"/>
          <w:rFonts w:hAnsi="Tw Cen MT" w:ascii="Tw Cen MT"/>
        </w:rPr>
        <w:t>https://www.najfnr.org</w:t>
      </w:r>
    </w:hyperlink>
    - <w:r w:rsidRPr="00B409E3">
      - <w:rPr>
        <w:rFonts w:hAnsi="Tw Cen MT" w:ascii="Tw Cen MT"/>
      </w:rPr>
      <w:t xml:space="preserve"></w:t>
    </w:r>
  </w:p>
</w:txbxContent>
</wps:txbx>
- <wps:bodyPr bIns="0" rIns="0" tIns="0" lIns="0" vert="horz" rtlCol="0"
  horzOverflow="overflow">
  <a:noAutofit/>
</wps:bodyPr>
</wps:wsp>
- <wps:wsp>
  <wps:cNvPr name="Rectangle 246" id="246"/>
  <wps:cNvSpPr/>
  - <wps:spPr>
    - <a:xfrm>
      <a:off y="697616" x="3882209"/>
      <a:ext cx="38021" cy="168235"/>
    </a:xfrm>
    - <a:prstGeom prst="rect">
      <a:avLst/>
    </a:prstGeom>
    - <a:ln>
      <a:noFill/>
    </a:ln>
  </wps:spPr>
- <wps:txbx>
  - <w:txbxContent>
    - <w:p w:rsidP="00C62C26" w:rsidRDefault="00F806F5" w:rsidR="00F806F5"
      w14:textId="77777777" w14:paraId="12DCABAE">
      - <w:pPr>
        <w:spacing w:lineRule="auto" w:line="259" w:after="160" w:before="0"/>
        <w:ind w:right="0" w:left="0" w:firstLine="0"/>
        <w:jc w:val="left"/>
      </w:pPr>
      - <w:r>
        <w:t xml:space="preserve"></w:t>
      </w:r>
    </w:p>
  </w:txbxContent>
</wps:txbx>
- <wps:bodyPr bIns="0" rIns="0" tIns="0" lIns="0" vert="horz" rtlCol="0"
  horzOverflow="overflow">
  <a:noAutofit/>
</wps:bodyPr>
</wps:wsp>
- <wps:wsp>
  <wps:cNvPr name="Rectangle 255" id="255"/>

```

```

<wps:cNvSpPr/>
- <wps:spPr>
  - <a:xfrm>
    <a:off y="906785" x="5902145"/>
    <a:ext cx="42144" cy="186477"/>
  </a:xfrm>
  - <a:prstGeom prst="rect">
    <a:avLst/>
  </a:prstGeom>
  - <a:ln>
    <a:noFill/>
  </a:ln>
</wps:spPr>
- <wps:txbx>
  - <w:txbxContent>
    - <w:p w:rsidP="00C62C26" w:rsidRDefault="00F806F5" w:rsidR="00F806F5"
      w14:textId="77777777" w14:paraId="0BB7595C">
        - <w:pPr>
          <w:spacing w:lineRule="auto" w:line="259" w:after="160" w:before="0"/>
          <w:ind w:right="0" w:left="0" w:firstLine="0"/>
          <w:jc w:val="left"/>
        </w:pPr>
        - <w:r>
          - <w:rPr>
            <w:sz w:val="22"/>
          </w:rPr>
          <w:t xml:space="preserve"></w:t>
        </w:r>
      </w:p>
    </w:txbxContent>
  </wps:txbx>
- <wps:bodyPr bInns="0" rInns="0" tInns="0" lInns="0" vert="horz" rtlCol="0"
  horzOverflow="overflow">
  <a:noAutofit/>
</wps:bodyPr>
</wps:wsp>
</wpg:wgp>
</a:graphicData>
</a:graphic>
</wp:inline>
</w:drawing>
</mc:Choice>
- <mc:Fallback>
  - <w:pict>
    - <v:group id="Group 10991" w14:anchorId="089BE259"
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      90jcwfiWJU67QAgI6YK0S0CoHGBkTxKLZGx5TGhv5O2G0SRWNoz/78nu9wcxkFMGNg6quQqL6RA
      0s5Y6ir5vt9ID1JwBDIwOMJKHpHlpr69KfdHjyxSmriSfYz+USnWPY7AufNIadK6MEJmX9ApD/oD
      OITrorhX2lFEilmcO2RdNtjC5xDEF9pCuTyYBB5bi6bQ4syoJ3g9WQ0ymailZg5KdCXIKLjvcW893
      SUOqXwnz5DrgnHtJTxOsQfEKIT7DmDSUCaxw7Rqn8787ZsmRM9e2VmPeBN4uqYvTtW7jvijg9N/y
      JsXecLq0q+WD6m8AAAD//wMAUEsDBBQABgAIAAAAIQA4/SH/1gAAAJQBAAALAAAAAX3JlbHMvLnJl
      bHOkkMFqzwAMhu+DvYPRfXGawxijTi+j0GvpHsDYimMaW0Yy2fr2M4PBMnrbUb/Q94l/fhMi1qR
      JVI2sOt6UJgd+ZiDgffl8ekFfSbvV0o4EbChzGx4f9GRdb25HMsYhqlCwG5lrLq9biZkxWOiqY
      22YiTra2kYMu1l1tQD30/bPm3wwYN0x18gb45AdQl1tp5j/FB2T0FQ7R0nTNEV3j6o9feQzro1i
      OWA14Fm+Q8a1a8+Bvu/d/dMb2JY5uiPbhG/ktm4cqGU/er3pcvwCAAD//wMAUEsDBBQABgAIAAAAI
      IQBRUXBwkAAAG4VAAAOAAAAAZHJzL2Uyb0RvYy54bWzkWG1v2zYQ/j5g/0Hq98Yi9W7EKYZ2CCQZs
      bdF2P4DRiy2AIGVSiz39+t0dRdmxg6HugKR0EsCijsfj3fOQ1B0v3+56Gdw3xnZarUJ2EYVBoypd
      d2q9Cv+ev2mCmAM7CIULqVWzCh8aG769+vWXY+2wbLjeaFk3JgAji63wyrjcjOOwXCxstWI6YS/0
      0CjobLXpxQivZr2ojdiC9V4ueBRli6029WB01VgLoveuM7wi+23bVOPHtrXNGMhVCL6N9Gvo9xZ/
      F1eXYrk2Yth01eSG+A4vetEpmHQ29V6MIrgz3YmpvquMtrodLyrL3TbdlVDMUA0LDqK5sbou4Fi
      WS+362GGCa9wum7zYfY7j+ZoKuBu6gsWRgo0QNNHPgRADRdlgvQfPGDF+GT2YSrN0bRr1rTY9P
      iCfYebgPM7jNbgwqEKZIUURpGgYV9LGIJQnjDv5qAxzhuDdJnGdZGIBCXGa88N2/P2mCcc5ZgjoL
      78ECHZ392g6wpuweNvv/YPuyEUNDbFgEw8OW5B60z7DahFrLJmAgJJRIc8bMLi3A9wRgvCyyJLCuP
      I/fQJRBnMgFXZEIOxuegxXIwdrxpdb9gYxUa8IMWo7j/044OH6+Ck0uFv0pfdn1K6XpQAdt4/bI27
      251bFz6SW10/QNAbbf75CDu+IXq7CvXUCvEQGLmxNwzkHwrAxv3mG8Y3bn3DjPKdpl3pvPntbtRt
      R+7i/G62yS1gERfhs9AJB5bbA4d001JEB4D48+hMozwpM7eSfwg+adPtef7p+YrRddcpn6Rf12XyW
      eRpn6Q/EZ+xDeRX7k8dP8InC45bVuaMPnbwoUlZzhP2mE+WfYwv4fiT1VW8JgIf64T175pr2aH
      8oSf7lAUsNonCZxUUD6goymaVEQhmLpT9y4iDj0vgvftHheDZ8sLvi8RylnCpzoHD4PMsEsjzkY
      hNF7OIGXZFE2pURwHOcZfIHG7S6cykRjvJpEGTntUulQLbxrWqnfBMTp/8sFAYx4jg0is0AEqA0
      yflkhyW8gaTVeYLdPSRGXzUpjkcpMXi575XqUGs2BsvYR+Q1/HMge4eajwDwav7p1OEsw6T6ECmv
      4J+Hio/nBocxWsqzZwRAel1bKrMaHeKl6a95JE9wLyPBEVTVqzCgllXf9X7p28ISCP0csiLEG
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" coordsize="5467472,365760"
style="position:absolute;left:-437;top:6732;width:59809;height:3657;visibility:visible;mso-wrap-
style:square;v-text-anchor:top" o:spid="_x0000_s1033">
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<v:path textboxrect="0,0,5467472,365760" arrowok="t"/>
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- <v:rect id="Rectangle 244" stroked="f"
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" style="position:absolute;left:18351;top:6973;width:29337;height:1682;visibility:visible;mso-wrap-
style:square;v-text-anchor:top" o:spid="_x0000_s1034" filled="f">
- <v:textbox inset="0,0,0,0">

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- <w:txbxContent>
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  - <w:pPr>
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    <w:ind w:right="0" w:left="0" w:firstLine="0"/>
    <w:jc w:val="left"/>
  - <w:rPr>
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  </w:rPr>
</w:pPr>
- <w:r w:rsidRPr="00B409E3">
  - <w:rPr>
    <w:rFonts w:hAnsi="Tw Cen MT" w:ascii="Tw Cen MT"/>
  </w:rPr>
  <w:t xml:space="preserve">Journal homepage: </w:t>
</w:r>
- <w:hyperlink r:id="rId12" w:history="1">
  - <w:r w:rsidRPr="00B409E3">
    - <w:rPr>
      <w:rStyle w:val="Hyperlink"/>
      <w:rFonts w:hAnsi="Tw Cen MT" w:ascii="Tw Cen MT"/>
    </w:rPr>
    <w:t>https://www.najfnr.org</w:t>
  </w:r>
</w:hyperlink>
- <w:r w:rsidRPr="00B409E3">
  - <w:rPr>
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- <v:rect id="Rectangle 246" stroked="f"
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  AAAAAAAAAAAAAAAAAAAHwEAAf9yZWxzLy5yZWxzUesBai0AFAAGAAgAAAAhAGLRCRnEAAAAA3AAA
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        - <w:pPr>
          <w:spacing w:lineRule="auto" w:line="259" w:after="160" w:before="0"/>
          <w:ind w:right="0" w:left="0" w:firstLine="0"/>
          <w:jc w:val="left"/>
        </w:pPr>
        - <w:r>
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        </w:r>
      </w:p>
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  </v:txbxContent>
</v:rect>
- <v:rect id="Rectangle 255" stroked="f"
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CwAAAAAAAAAAAAAAAAAfaQAAX3JlbHMvLnJlbHNQSwECLQAUAAYACAAAACEAF9oBs8YAAADc
DwAAAAAAAAAAAAAAAAAAHAgAAZHJzL2Rvd25yZXYueG1sUEsFBgAAAAADAAMAtwAAAPoCAAAA/

" style="position:absolute;left:59021;top:9067;width:421;height:1865;visibility:visible;mso-wrap-
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- <v:textbox inset="0,0,0,0">

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</v:textbox>

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</v:group>

</w:pict>

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</w:p>

- <w:p w:rsidP="00C62C26" w:rsidRDefault="002823BD" w:rsidR="00C62C26" w14:textId="77777777" w14:paraId="65CF3ED2" w:rsidRPr="005C028C">

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<w:jc w:val="center"/>

- <w:rPr>

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<w:sz w:val="30"/>

<w:szCs w:val="30"/>

</w:rPr>

</w:pPr>

- <w:r w:rsidRPr="002823BD">

- <w:rPr>

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</w:rPr>

<w:t>Association between carotenoids and prostate cancer risk: A Meta-Analysis</w:t>

</w:r>

</w:p>

- <w:p w:rsidP="008A748A" w:rsidRDefault="008A748A" w:rsidR="00C62C26" w14:textId="77777777" w14:paraId="5AA9E311">

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</w:rPr>

</w:pPr>

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- <w:r w:rsidRPr="008A748A">

- <w:rPr>

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</w:rPr>

<w:t>Hadjer</w:t>

</w:r>

<w:proofErr w:type="spellEnd"/>


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</w:r>
- <w:r w:rsidRPr="008A748A">
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- <w:r w:rsidRPr="008A748A">
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  </w:rPr>
  <w:t xml:space="preserve">, Manel BOUCHENTOUF </w:t>
</w:r>
- <w:r w:rsidRPr="008A748A">
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    <w:rFonts w:hAnsiTheme="minorBidi" w:asciiTheme="minorBidi"/>
    <w:color w:val="000000" w:themeColor="text1"/>
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  <w:t>1</w:t>
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    <w:rFonts w:hAnsiTheme="minorBidi" w:asciiTheme="minorBidi"/>
    <w:b/>
    <w:bCs/>
    <w:color w:val="000000" w:themeColor="text1"/>
    <w:u w:val="single"/>
  </w:rPr>
  <w:t xml:space="preserve">Salah Eddine EL </w:t>
</w:r>
- <w:r w:rsidRPr="00092705">
  - <w:rPr>
    <w:rFonts w:hAnsiTheme="minorBidi" w:asciiTheme="minorBidi"/>
    <w:b/>
    <w:bCs/>
    <w:noProof/>
    <w:color w:val="000000" w:themeColor="text1"/>
    <w:u w:val="single"/>
  </w:rPr>
  <w:t>HERRAG</w:t>
</w:r>
- <w:r w:rsidRPr="008A748A">
  - <w:rPr>
    <w:rFonts w:hAnsiTheme="minorBidi" w:asciiTheme="minorBidi"/>
    <w:b/>
    <w:bCs/>
    <w:color w:val="000000" w:themeColor="text1"/>
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- <w:r w:rsidRPr="008A748A">
  - <w:rPr>
    <w:rFonts w:hAnsiTheme="minorBidi" w:asciiTheme="minorBidi"/>
    <w:b/>
    <w:bCs/>
    <w:color w:val="000000" w:themeColor="text1"/>
    <w:vertAlign w:val="superscript"/>
  </w:rPr>
  <w:t xml:space="preserve">1 </w:t>
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  - <w:rPr>
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  w:rsidRPr="00DD0224">
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    <w:jc w:val="center"/>
    - <w:rPr>
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      <w:sz w:val="16"/>
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    </w:rPr>
  </w:pPr>
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      <w:sz w:val="16"/>
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  </w:pPr>
  - <w:r>
    - <w:rPr>
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      <w:bCs/>
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    </w:rPr>
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  </w:r>
  - <w:r w:rsidR="00C62C26" w:rsidRPr="00C35468">
    - <w:rPr>
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      <w:bCs/>
      <w:sz w:val="16"/>
      <w:szCs w:val="16"/>
    </w:rPr>
    <w:t xml:space="preserve">Department of Biology, Faculty of Natural and Life Sciences, Djillali Liabes University, PO Box 89, Sidi-
      Bel-Abbes (22000), Algeria</w:t>
  </w:r>
</w:p>
- <w:tbl>
  - <w:tblPr>
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    <w:tblPr w:tblpY="564" w:tblpX="240" w:vertAnchor="text"/>
    <w:tblOverlap w:val="never"/>
    <w:tblW w:w="5130" w:type="dxa"/>
    <w:tblInd w:w="0" w:type="dxa"/>
    <w:tblLook w:val="04A0" w:noVBand="1" w:noHBand="0" w:lastColumn="0" w:firstColumn="1" w:lastRow="0" w:firstRow="1"/>
  </w:tblPr>
  - <w:tblGrid>
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  </w:tblGrid>
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    - <w:tc>
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      - <w:tcBorders>
        <w:top w:val="nil"/>
        <w:left w:val="nil"/>
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  <w:jc w:val="left"/>
- <w:rPr>
  <w:rFonts w:hAnsi="Tw Cen MT" w:ascii="Tw Cen MT"/>
  <w:b/>
  <w:bCs/>
</w:rPr>
</w:pPr>
</w:p>
- <w:p w:rsidP="008B0DCA" w:rsidRDefault="008B0DCA" w:rsidR="00C62C26" w14:textId="77777777"
w14:paraId="6F4DDC83" w:rsidRPr="008B0DCA">
- <w:pPr>
  <w:spacing w:lineRule="auto" w:line="240" w:after="0" w:before="0"/>
  <w:ind w:right="0" w:left="0" w:firstLine="0"/>
  <w:contextualSpacing/>
  <w:jc w:val="left"/>
- <w:rPr>
  <w:rFonts w:cs="Times New Roman" w:hAnsi="Times New Roman" w:ascii="Times New Roman"/>
</w:rPr>
</w:pPr>
- <w:r w:rsidRPr="00695689">
- <w:rPr>
  <w:rFonts w:cs="Times New Roman" w:hAnsi="Times New Roman" w:ascii="Times New Roman"/>
  <w:noProof/>
</w:rPr>
<w:t>A R</w:t>
</w:r>
- <w:r w:rsidRPr="00C11383">
- <w:rPr>
  <w:rFonts w:cs="Times New Roman" w:hAnsi="Times New Roman" w:ascii="Times New Roman"/>
</w:rPr>
<w:t xml:space="preserve">T I C L E</w:t>
</w:r>
- <w:r>
- <w:rPr>
  <w:rFonts w:cs="Times New Roman" w:hAnsi="Times New Roman" w:ascii="Times New Roman"/>
</w:rPr>
<w:t xml:space="preserve">I N F O</w:t>
</w:r>
- <w:r w:rsidR="00C62C26" w:rsidRPr="005C028C">
  <w:t xml:space="preserve"></w:t>
</w:r>
</w:p>
</w:tc>
- <w:tc>
- <w:tcPr>
  <w:tcW w:w="264" w:type="dxa"/>
- <w:tcBorders>
  <w:top w:val="nil"/>
  <w:left w:val="nil"/>
  <w:bottom w:val="nil"/>
  <w:right w:val="nil"/>
</w:tcBorders>
  <w:vAlign w:val="bottom"/>
</w:tcPr>
- <w:p w:rsidP="009B08AB" w:rsidRDefault="00C62C26" w:rsidR="00C62C26" w14:textId="77777777" w14:paraId="19116FE6"
w:rsidRPr="005C028C">
- <w:pPr>
  <w:spacing w:lineRule="auto" w:line="240" w:after="0" w:before="0"/>
  <w:ind w:right="0" w:left="0" w:firstLine="0"/>
  <w:contextualSpacing/>
  <w:jc w:val="left"/>
</w:pPr>
- <w:r w:rsidRPr="005C028C">
  <w:t xml:space="preserve"></w:t>
</w:r>
</w:p>
</w:tc>
- <w:tc>
- <w:tcPr>
  <w:tcW w:w="1424" w:type="dxa"/>
- <w:tcBorders>
  <w:top w:val="nil"/>
  <w:left w:val="nil"/>
  <w:bottom w:val="nil"/>
  <w:right w:val="nil"/>
</w:tcBorders>
</w:tcPr>
-

```



```

<w:p w:rsidP="009B08AB" w:rsidRDefault="00C62C26" w:rsidR="00C62C26" w14:textId="77777777" w14:paraId="4CFE8A05"
w:rsidRPr="00611197">
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    <w:ind w:right="0" w:left="0" w:firstLine="0"/>
    <w:contextualSpacing/>
    - <w:rPr>
      <w:rFonts w:hAnsi="Tw Cen MT" w:ascii="Tw Cen MT"/>
      <w:b/>
      <w:bCs/>
      <w:sz w:val="18"/>
      <w:szCs w:val="18"/>
    </w:rPr>
  </w:pPr>
</w:p>
- <w:p w:rsidP="008F595A" w:rsidRDefault="008F595A" w:rsidR="00C62C26" w14:textId="77777777" w14:paraId="5C01B5E2"
w:rsidRPr="008F595A">
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    <w:ind w:right="0" w:left="0" w:firstLine="0"/>
    <w:contextualSpacing/>
    - <w:rPr>
      <w:rFonts w:hAnsi="Bell MT" w:ascii="Bell MT"/>
    </w:rPr>
  </w:pPr>
  - <w:r w:rsidRPr="00C11383">
    - <w:rPr>
      <w:rFonts w:hAnsi="Bell MT" w:ascii="Bell MT"/>
    </w:rPr>
    <w:t xml:space="preserve">A B S T R A C T </w:t>
  </w:r>
  - <w:r w:rsidR="00C62C26" w:rsidRPr="005C028C">
    <w:t xml:space="preserve"></w:t>
  </w:r>
</w:p>
</w:tr>
</w:tbl>
- <w:tbl>
  - <w:tblPr>
    <w:tblStyle w:val="TableGrid0"/>
    <w:tblPr w:tblpY="1306" w:tblpX="90" w:vertAnchor="text" w:horzAnchor="margin" w:rightFromText="180"
w:leftFromText="180"/>
    <w:tblW w:w="9490" w:type="dxa"/>
  - <w:tblBorders>
    <w:top w:val="none" w:space="0" w:color="auto" w:sz="0"/>
    <w:left w:val="none" w:space="0" w:color="auto" w:sz="0"/>
    <w:bottom w:val="none" w:space="0" w:color="auto" w:sz="0"/>
    <w:right w:val="none" w:space="0" w:color="auto" w:sz="0"/>
    <w:insideH w:val="none" w:space="0" w:color="auto" w:sz="0"/>
    <w:insideV w:val="none" w:space="0" w:color="auto" w:sz="0"/>
  </w:tblBorders>
  <w:tblLook w:val="04A0" w:noVBand="1" w:noHBand="0" w:lastColumn="0" w:firstColumn="1" w:lastRow="0" w:firstRow="1"/>
</w:tblPr>
- <w:tblGrid>
  <w:gridCol w:w="3701"/>
  <w:gridCol w:w="5789"/>
</w:tblGrid>
- <w:tr w:rsidR="00C62C26" w14:textId="77777777" w14:paraId="43DDD236" w:rsidTr="00033A39">
  - <w:tc>
    - <w:tcPr>
      <w:tcW w:w="3701" w:type="dxa"/>
    </w:tcPr>
    - <w:p w:rsidP="00033A39" w:rsidRDefault="00C62C26" w:rsidR="00C62C26" w14:textId="77777777" w14:paraId="79E61232"
w:rsidRPr="005C028C">
      - <w:pPr>
        <w:spacing w:lineRule="auto" w:line="259" w:after="0" w:before="0"/>
        <w:ind w:right="0" w:left="0" w:firstLine="0"/>
        <w:jc w:val="left"/>
        - <w:rPr>
          <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Tw Cen MT" w:ascii="Tw Cen MT"/>
          <w:b/>
          <w:bCs/>
          <w:iCs/>
          <w:sz w:val="14"/>
          <w:szCs w:val="14"/>
        </w:rPr>
      </w:pPr>
      - <w:r w:rsidRPr="005C028C">
        - <w:rPr>
          <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Tw Cen MT" w:ascii="Tw Cen MT"/>
          <w:b/>

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        <w:bCs/>
        <w:iCs/>
        <w:sz w:val="14"/>
        <w:szCs w:val="14"/>
    </w:rPr>
    <w:t xml:space="preserve">Article history: </w:t>
</w:r>
</w:p>
- <w:p w:rsidP="00033A39" w:rsidRDefault="002D35A0" w:rsidR="002D35A0" w14:textId="77777777" w14:paraId="0A550646"
  w:rsidRPr="005C028C">
  - <w:pPr>
    <w:spacing w:lineRule="auto" w:line="259" w:after="0" w:before="0"/>
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    <w:jc w:val="left"/>
  - <w:rPr>
    <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI
      Semilight"/>
    <w:sz w:val="14"/>
    <w:szCs w:val="14"/>
  </w:rPr>
</w:pPr>
- <w:r>
  - <w:rPr>
    <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI
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    <w:szCs w:val="14"/>
  </w:rPr>
  <w:t>Received</w:t>
</w:r>
- <w:r w:rsidRPr="005C028C">
  - <w:rPr>
    <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI
      Semilight"/>
    <w:sz w:val="14"/>
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  </w:rPr>
  <w:t xml:space="preserve"></w:t>
</w:r>
- <w:r w:rsidR="00776EF9">
  - <w:rPr>
    <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI
      Semilight"/>
    <w:sz w:val="14"/>
    <w:szCs w:val="14"/>
  </w:rPr>
  <w:t>11 November</w:t>
</w:r>
- <w:r>
  - <w:rPr>
    <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI
      Semilight"/>
    <w:sz w:val="14"/>
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  </w:rPr>
  <w:t xml:space="preserve"></w:t>
</w:r>
- <w:r w:rsidRPr="005C028C">
  - <w:rPr>
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      Semilight"/>
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    <w:szCs w:val="14"/>
  </w:rPr>
  <w:t>201</w:t>
</w:r>
- <w:r>
  - <w:rPr>
    <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI
      Semilight"/>
    <w:sz w:val="14"/>
    <w:szCs w:val="14"/>
  </w:rPr>
  <w:t>8</w:t>
</w:r>
- <w:r w:rsidRPr="005C028C">
  - <w:rPr>
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      Semilight"/>
    <w:sz w:val="14"/>
    <w:szCs w:val="14"/>
  </w:rPr>

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        <w:t xml:space="preserve"></w:t>
      </w:r>
    </w:p>
  - <w:p w:rsidP="00033A39" w:rsidRDefault="00776EF9" w:rsidR="002D35A0" w14:textId="77777777" w14:paraId="7ADE5383"
    w:rsidRPr="005C028C">
    - <w:pPr>
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      <w:ind w:right="0" w:left="0" w:firstLine="0"/>
      <w:jc w:val="left"/>
    - <w:rPr>
      <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI
        Semilight"/>
      <w:sz w:val="14"/>
      <w:szCs w:val="14"/>
    </w:rPr>
  </w:pPr>
- <w:r>
  - <w:rPr>
    <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI
      Semilight"/>
    <w:sz w:val="14"/>
    <w:szCs w:val="14"/>
  </w:rPr>
  <w:t>Accepted 20 January</w:t>
</w:r>
- <w:r w:rsidR="002D35A0" w:rsidRPr="005C028C">
  - <w:rPr>
    <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI
      Semilight"/>
    <w:sz w:val="14"/>
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  </w:rPr>
  <w:t xml:space="preserve"> 201</w:t>
</w:r>
- <w:r>
  - <w:rPr>
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      Semilight"/>
    <w:sz w:val="14"/>
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  </w:rPr>
  <w:t>9</w:t>
</w:r>
- <w:r w:rsidR="002D35A0" w:rsidRPr="005C028C">
  - <w:rPr>
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    <w:sz w:val="14"/>
    <w:szCs w:val="14"/>
  </w:rPr>
  <w:t xml:space="preserve"></w:t>
</w:r>
</w:p>
- <w:p w:rsidP="00776EF9" w:rsidRDefault="002D35A0" w:rsidR="00C62C26" w14:textId="77777777" w14:paraId="3E36CF9C"
  w:rsidRPr="005C028C">
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    <w:jc w:val="left"/>
  - <w:rPr>
    <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI
      Semilight"/>
    <w:sz w:val="14"/>
    <w:szCs w:val="14"/>
  </w:rPr>
</w:pPr>
- <w:r>
  - <w:rPr>
    <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI
      Semilight"/>
    <w:sz w:val="14"/>
    <w:szCs w:val="14"/>
  </w:rPr>
  <w:t xml:space="preserve">Available online</w:t>
</w:r>
- <w:r w:rsidR="00ED042C">
  - <w:rPr>
    <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI
      Semilight"/>
    <w:sz w:val="14"/>
    <w:szCs w:val="14"/>
  </w:rPr>

```

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      </w:r>
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      - <w:rPr>
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        <w:szCs w:val="14"/>
      </w:rPr>
      <w:t>February</w:t>
    </w:r>
    - <w:r w:rsidRPr="005C028C">
      - <w:rPr>
        <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI Semilight"/>
        <w:sz w:val="14"/>
        <w:szCs w:val="14"/>
      </w:rPr>
      <w:t xml:space="preserve"></w:t>
    </w:r>
    - <w:r w:rsidR="00776EF9">
      - <w:rPr>
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      <w:t>2019</w:t>
    </w:r>
  </w:p>
  - <w:p w:rsidP="00033A39" w:rsidRDefault="00C62C26" w:rsidR="00C62C26" w14:textId="77777777" w14:paraId="57C779CC" w:rsidRPr="005C028C">
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      <w:jc w:val="left"/>
    - <w:rPr>
      <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Tw Cen MT" w:ascii="Tw Cen MT"/>
      <w:b/>
      <w:bCs/>
      <w:iCs/>
      <w:sz w:val="14"/>
      <w:szCs w:val="14"/>
    </w:rPr>
  </w:pPr>
  - <w:r w:rsidRPr="005C028C">
    - <w:rPr>
      <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Tw Cen MT" w:ascii="Tw Cen MT"/>
      <w:b/>
      <w:bCs/>
      <w:iCs/>
      <w:sz w:val="14"/>
      <w:szCs w:val="14"/>
    </w:rPr>
    <w:t xml:space="preserve">Keywords: </w:t>
  </w:r>
</w:p>
  - <w:p w:rsidP="00033A39" w:rsidRDefault="00340EA0" w:rsidR="00C62C26" w14:textId="77777777" w14:paraId="1A98770E" w:rsidRPr="005C028C">
    - <w:pPr>
      <w:spacing w:lineRule="auto" w:line="259" w:after="0" w:before="0"/>
      <w:ind w:right="0" w:left="0" w:firstLine="0"/>
      <w:jc w:val="left"/>
    - <w:rPr>
      <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI Semilight"/>
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      <w:szCs w:val="14"/>
    </w:rPr>
  </w:pPr>
  - <w:r w:rsidRPr="00340EA0">
    - <w:rPr>
      <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI Semilight"/>
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      <w:szCs w:val="14"/>
    </w:rPr>
    <w:t>Prostate cancer</w:t>
  </w:r>
</w:p>

```

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<w:p w:rsidP="00340EA0" w:rsidRDefault="00340EA0" w:rsidR="00C62C26" w14:textId="77777777" w14:paraId="661C15CC"
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    <w:jc w:val="left"/>
    - <w:rPr>
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      Semilight"/>
      <w:sz w:val="14"/>
      <w:szCs w:val="14"/>
    </w:rPr>
  </w:pPr>
  - <w:r>
    - <w:rPr>
      <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI
      Semilight"/>
      <w:bCs/>
      <w:sz w:val="14"/>
      <w:szCs w:val="14"/>
    </w:rPr>
    <w:t>C</w:t>
  </w:r>
  - <w:r w:rsidRPr="00340EA0">
    - <w:rPr>
      <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI
      Semilight"/>
      <w:bCs/>
      <w:sz w:val="14"/>
      <w:szCs w:val="14"/>
    </w:rPr>
    <w:t>arotenoids</w:t>
  </w:r>
</w:p>
- <w:p w:rsidP="00340EA0" w:rsidRDefault="00340EA0" w:rsidR="00C62C26" w14:textId="77777777" w14:paraId="5E7D1869"
w:rsidRPr="005C028C">
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    <w:ind w:right="0" w:left="0" w:firstLine="0"/>
    <w:jc w:val="left"/>
    - <w:rPr>
      <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI
      Semilight"/>
      <w:sz w:val="14"/>
      <w:szCs w:val="14"/>
    </w:rPr>
  </w:pPr>
  - <w:r>
    - <w:rPr>
      <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI
      Semilight"/>
      <w:bCs/>
      <w:sz w:val="14"/>
      <w:szCs w:val="14"/>
    </w:rPr>
    <w:t>L</w:t>
  </w:r>
  - <w:r w:rsidRPr="00340EA0">
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      Semilight"/>
      <w:bCs/>
      <w:sz w:val="14"/>
      <w:szCs w:val="14"/>
    </w:rPr>
    <w:t>ycopene</w:t>
  </w:r>
  - <w:r>
    - <w:rPr>
      <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI
      Semilight"/>
      <w:bCs/>
      <w:sz w:val="14"/>
      <w:szCs w:val="14"/>
    </w:rPr>
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    - <w:rPr>
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      <w:szCs w:val="14"/>
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```

        </w:rPr>
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    </w:r>
    - <w:r w:rsidRPr="00340EA0">
        - <w:rPr>
            <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI Semilight"/>
            <w:bCs/>
            <w:sz w:val="14"/>
            <w:szCs w:val="14"/>
        </w:rPr>
        <w:t>-Carotene</w:t>
    </w:r>
</w:p>
- <w:p w:rsidP="00340EA0" w:rsidRDefault="00340EA0" w:rsidR="00C62C26" w14:textId="77777777" w14:paraId="001E642B">
    - <w:pPr>
        <w:spacing w:lineRule="auto" w:line="259" w:after="0" w:before="0"/>
        <w:ind w:right="0" w:left="0" w:firstLine="0"/>
        <w:jc w:val="left"/>
    - <w:rPr>
        <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI Semilight"/>
        <w:sz w:val="14"/>
        <w:szCs w:val="14"/>
    </w:rPr>
</w:pPr>
- <w:r w:rsidRPr="00340EA0">
    - <w:rPr>
        <w:bCs/>
        <w:sz w:val="14"/>
        <w:szCs w:val="14"/>
    </w:rPr>
    <w:t>α</w:t>
</w:r>
- <w:r w:rsidRPr="00340EA0">
    - <w:rPr>
        <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI Semilight"/>
        <w:bCs/>
        <w:sz w:val="14"/>
        <w:szCs w:val="14"/>
    </w:rPr>
    <w:t>-Carotene</w:t>
</w:r>
- <w:r>
    - <w:rPr>
        <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI Semilight"/>
        <w:bCs/>
        <w:sz w:val="14"/>
        <w:szCs w:val="14"/>
    </w:rPr>
    <w:t xml:space="preserve">, </w:t>
</w:r>
- <w:r w:rsidRPr="00340EA0">
    - <w:rPr>
        <w:bCs/>
        <w:sz w:val="14"/>
        <w:szCs w:val="14"/>
    </w:rPr>
    <w:t>β</w:t>
</w:r>
- <w:r w:rsidRPr="00340EA0">
    - <w:rPr>
        <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI Semilight"/>
        <w:bCs/>
        <w:sz w:val="14"/>
        <w:szCs w:val="14"/>
    </w:rPr>
    <w:t>-cryptoxanthin</w:t>
</w:r>
</w:p>
- <w:p w:rsidP="00340EA0" w:rsidRDefault="00340EA0" w:rsidR="00132E91" w14:textId="77777777" w14:paraId="28F567F1">
    - <w:pPr>
        <w:spacing w:lineRule="auto" w:line="259" w:after="0" w:before="0"/>
        <w:ind w:right="0" w:left="0" w:firstLine="0"/>
        <w:jc w:val="left"/>
    - <w:rPr>
        <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI Semilight"/>
        <w:sz w:val="14"/>

```

```

        <w:szCs w:val="14"/>
      </w:rPr>
    </w:pPr>
  - <w:r>
    - <w:rPr>
      <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI Semilight"/>
      <w:bCs/>
      <w:sz w:val="14"/>
      <w:szCs w:val="14"/>
    </w:rPr>
    <w:t>L</w:t>
  </w:r>
  - <w:r w:rsidRPr="00340EA0">
    - <w:rPr>
      <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI Semilight"/>
      <w:bCs/>
      <w:sz w:val="14"/>
      <w:szCs w:val="14"/>
    </w:rPr>
    <w:t>utein/zeaxanthin</w:t>
  </w:r>
  - <w:r w:rsidR="002D35A0">
    - <w:rPr>
      <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI Semilight"/>
      <w:sz w:val="14"/>
      <w:szCs w:val="14"/>
    </w:rPr>
    <w:t>,</w:t>
  </w:r>
</w:p>
- <w:p w:rsidP="00340EA0" w:rsidRDefault="002D35A0" w:rsidR="00C62C26" w14:textId="77777777" w14:paraId="69A1435E">
  - <w:pPr>
    <w:spacing w:lineRule="auto" w:line="259" w:after="0" w:before="0"/>
    <w:ind w:right="0" w:left="0" w:firstLine="0"/>
    <w:jc w:val="left"/>
  - <w:rPr>
    <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI Semilight"/>
    <w:sz w:val="14"/>
    <w:szCs w:val="14"/>
  </w:rPr>
  - <w:r w:rsidRPr="00577ADA">
    - <w:rPr>
      <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI Semilight"/>
      <w:sz w:val="14"/>
      <w:szCs w:val="14"/>
    </w:rPr>
    <w:t>Meta-analysis</w:t>
  </w:r>
  - <w:r>
    - <w:rPr>
      <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI Semilight"/>
      <w:sz w:val="14"/>
      <w:szCs w:val="14"/>
    </w:rPr>
    <w:t>.</w:t>
  </w:r>
</w:p>
- <w:tbl>
  - <w:tblPr>
    <w:tblStyle w:val="TableGrid0"/>
    <w:tblpPr w:tblpY="228" w:vertAnchor="text" w:horzAnchor="margin" w:rightFromText="180" w:leftFromText="180"/>
    <w:tblOverlap w:val="never"/>
    <w:tblW w:w="0" w:type="auto"/>
    <w:tblLook w:val="04A0" w:noVBand="1" w:noHBand="0" w:lastColumn="0" w:firstColumn="1" w:lastRow="0" w:firstRow="1"/>
  </w:tblPr>
  - <w:tblGrid>
    <w:gridCol w:w="1615"/>
    <w:gridCol w:w="1620"/>
  </w:tblGrid>
  - <w:tr w:rsidR="002D35A0" w14:textId="77777777" w14:paraId="741349D2" w:rsidRPr="005C028C" w:rsidTr="0099201C">
    - <w:tc>
      - <w:tcPr>
        <w:tcW w:w="3235" w:type="dxa"/>

```



```

        <w:gridSpan w:val="2"/>
        <w:shd w:val="clear" w:color="auto" w:themeFillShade="BF" w:themeFill="accent6" w:fill="538135"/>
    </w:tcPr>
    - <w:p w:rsidP="00033A39" w:rsidRDefault="002D35A0" w:rsidR="002D35A0" w14:textId="77777777"
      w14:paraId="6AA26BED" w:rsidRPr="005C028C">
      - <w:pPr>
        <w:autoSpaceDE w:val="0"/>
        <w:autoSpaceDN w:val="0"/>
        <w:adjustRightInd w:val="0"/>
        <w:snapToGrid w:val="0"/>
        <w:spacing w:lineRule="auto" w:line="240" w:after="0" w:before="0"/>
        <w:ind w:right="0" w:left="0" w:firstLine="0"/>
        <w:jc w:val="center"/>
      - <w:rPr>
        <w:rFonts w:hAnsi="Tw Cen MT" w:ascii="Tw Cen MT"/>
        <w:b/>
        <w:bCs/>
        <w:color w:val="FFFFFF" w:themeColor="background1"/>
      </w:rPr>
    </w:pPr>
    - <w:r w:rsidRPr="005C028C">
      - <w:rPr>
        <w:rFonts w:cs="Arial-BoldMT" w:hAnsi="Tw Cen MT" w:ascii="Tw Cen MT" w:eastAsia="Times
          New Roman"/>
        <w:b/>
        <w:bCs/>
        <w:color w:val="FFFFFF" w:themeColor="background1"/>
        <w:sz w:val="14"/>
        <w:szCs w:val="24"/>
      </w:rPr>
      <w:t>Access this article online</w:t>
    </w:r>
  </w:p>
</w:tc>
</w:tr>
- <w:tr w:rsidR="002D35A0" w14:textId="77777777" w14:paraId="082B260A" w:rsidRPr="005C028C" w:rsidTr="0099201C">
  - <w:trPr>
    <w:trHeight w:val="202"/>
  </w:trPr>
  - <w:tc>
    - <w:tcPr>
      <w:tcW w:w="1615" w:type="dxa"/>
    </w:tcPr>
    - <w:p w:rsidP="00033A39" w:rsidRDefault="002D35A0" w:rsidR="002D35A0" w14:textId="77777777"
      w14:paraId="2303FE9E" w:rsidRPr="005C028C">
      - <w:pPr>
        <w:autoSpaceDE w:val="0"/>
        <w:autoSpaceDN w:val="0"/>
        <w:adjustRightInd w:val="0"/>
        <w:snapToGrid w:val="0"/>
        <w:spacing w:lineRule="auto" w:line="240" w:after="0" w:before="0"/>
        <w:ind w:right="0" w:left="0" w:firstLine="0"/>
        <w:jc w:val="center"/>
      - <w:rPr>
        <w:rFonts w:hAnsi="Tw Cen MT" w:ascii="Tw Cen MT"/>
      </w:rPr>
    </w:pPr>
    - <w:r w:rsidRPr="005C028C">
      - <w:rPr>
        <w:rFonts w:cs="Arial-BoldMT" w:hAnsi="Tw Cen MT" w:ascii="Tw Cen MT" w:eastAsia="Times
          New Roman"/>
        <w:sz w:val="14"/>
        <w:szCs w:val="24"/>
      </w:rPr>
      <w:t>Quick Response Code</w:t>
    </w:r>
    - <w:r w:rsidRPr="005C028C">
      - <w:rPr>
        <w:rFonts w:hAnsi="Tw Cen MT" w:ascii="Tw Cen MT"/>
      </w:rPr>
      <w:t>:</w:t>
    </w:r>
  </w:p>
</w:tc>
- <w:tc>
  - <w:tcPr>
    <w:tcW w:w="1620" w:type="dxa"/>
    <w:vMerge w:val="restart"/>
  </w:tcPr>
  - <w:p w:rsidP="00033A39" w:rsidRDefault="002D35A0" w:rsidR="002D35A0" w14:textId="77777777"
    w14:paraId="6B4BBAA7" w:rsidRPr="005C028C">
    - <w:pPr>

```

```

        <w:spacing w:lineRule="auto" w:line="259" w:after="0" w:before="0"/>
        <w:ind w:right="0" w:left="0" w:firstLine="0"/>
        <w:jc w:val="left"/>
    - <w:rPr>
        <w:rFonts w:hAnsi="Tw Cen MT" w:ascii="Tw Cen MT"/>
        <w:b/>
        <w:bCs/>
        <w:sz w:val="18"/>
        <w:szCs w:val="18"/>
    </w:rPr>
</w:pPr>
- <w:r w:rsidRPr="005C028C">
    - <w:rPr>
        <w:rFonts w:hAnsi="Tw Cen MT" w:ascii="Tw Cen MT"/>
        <w:b/>
        <w:bCs/>
        <w:sz w:val="18"/>
        <w:szCs w:val="18"/>
    </w:rPr>
    <w:t xml:space="preserve">Website: </w:t>
</w:r>
</w:p>
- <w:p w:rsidP="00033A39" w:rsidRDefault="002D35A0" w:rsidR="002D35A0" w14:textId="77777777"
w14:paraId="53448EE7" w:rsidRPr="005C028C">
    - <w:pPr>
        <w:spacing w:lineRule="auto" w:line="259" w:after="0" w:before="0"/>
        <w:ind w:right="0" w:left="0" w:firstLine="0"/>
        <w:jc w:val="left"/>
    - <w:rPr>
        <w:rFonts w:hAnsi="Tw Cen MT" w:ascii="Tw Cen MT"/>
        <w:sz w:val="18"/>
        <w:szCs w:val="18"/>
    </w:rPr>
</w:pPr>
- <w:r w:rsidRPr="005C028C">
    - <w:rPr>
        <w:rFonts w:hAnsi="Century Gothic" w:ascii="Century Gothic"/>
        <w:b/>
        <w:noProof/>
        <w:color w:val="385623" w:themeShade="80" w:themeColor="accent6"/>
        <w:sz w:val="30"/>
        <w:szCs w:val="30"/>
    </w:rPr>
    - <mc:AlternateContent>
        - <mc:Choice Requires="wps">
            - <w:drawing>
                - <wp:anchor wp14:editId="78764A35" wp14:anchorId="46B71390" allowOverlap="1"
layoutInCell="1" locked="0" behindDoc="0" relativeHeight="251705344" simplePos="0"
distR="114300" distL="114300" distB="45720" distT="45720">
                    <wp:simplePos y="0" x="0"/>
                    - <wp:positionH relativeFrom="margin">
                        <wp:posOffset>-36194</wp:posOffset>
                    </wp:positionH>
                    - <wp:positionV relativeFrom="paragraph">
                        <wp:posOffset>280035</wp:posOffset>
                    </wp:positionV>
                    <wp:extent cx="863600" cy="252442"/>
                    <wp:effectExtent r="0" b="0" t="0" l="0"/>
                    <wp:wrapNone/>
                    <wp:docPr name="Text Box 2" id="4"/>
                - <wp:cNvGraphicFramePr>
                    <a:graphicFrameLocks
xmlns:a="http://schemas.openxmlformats.org/drawingml/2006/main"/>
                </wp:cNvGraphicFramePr>
                - <a:graphic xmlns:a="http://schemas.openxmlformats.org/drawingml/2006/main">
                    - <a:graphicData
uri="http://schemas.microsoft.com/office/word/2010/wordprocessingShape">
                        - <wps:wsp>
                            - <wps:cNvSpPr txBox="1">
                                <a:spLocks noChangeArrowheads="1"/>
                            </wps:cNvSpPr>
                            - <wps:spPr bwMode="auto">
                                - <a:xfrm>
                                    <a:off y="0" x="0"/>
                                    <a:ext cx="863600" cy="252442"/>
                                </a:xfrm>
                                - <a:prstGeom prst="rect">
                                    <a:avLst/>
                                </a:prstGeom>
                                - <a:solidFill>
                                    <a:srgbClr val="FFFFFF"/>
                                </a:solidFill>

```

```

- <a:ln w="9525">
  <a:noFill/>
  <a:miter lim="800000"/>
  <a:headEnd/>
  <a:tailEnd/>
</a:ln>
</wps:spPr>
- <wps:txbx>
  - <w:txbxContent>
    - <w:p w:rsidP="002D35A0" w:rsidRDefault="00F806F5"
      w:rsidR="00F806F5" w14:textId="77777777"
      w14:paraId="574528B8" w:rsidRPr="00847784">
        - <w:pPr>
          <w:spacing w:lineRule="auto" w:line="240"
            w:after="0" w:before="0"/>
          <w:ind w:left="11" w:hanging="11"/>
          <w:jc w:val="right"/>
        - <w:rPr>
          <w:lang w:val="fr-FR"/>
        </w:rPr>
      </w:pPr>
    - <w:r>
      - <w:rPr>
        <w:noProof/>
      </w:rPr>
    - <w:drawing>
      - <wp:inline wp14:editId="1D4CC746"
        wp14:anchorId="4C4C119E" distR="0"
        distL="0" distB="0" distT="0">
        <wp:extent cx="673100" cy="241300"/>
        <wp:effectExtent r="0" b="6350" t="0"
          l="0"/>
        <wp:docPr name="Picture 11" id="11"/>
      - <wp:cNvGraphicFramePr>
        <a:graphicFrameLocks
          noChangeAspect="1"
          xmlns:a="http://schemas.openxml"
        </wp:cNvGraphicFramePr>
      - <a:graphic
        xmlns:a="http://schemas.openxmlformats.o
      - <a:graphicData
        uri="http://schemas.openxmlformats.o
      - <pic:pic
        xmlns:pic="http://schemas.openxm
      - <pic:nvPicPr>
        <pic:cNvPr
          name="Picture 1"
          id="0"/>
      - <pic:cNvPicPr>
        <a:picLocks
          noChangeAspe
          noChangeArro
        </pic:cNvPicPr>
      </pic:nvPicPr>
      - <pic:blipFill>
        - <a:blip
          r:embed="rId13">
          - <a:extLst>
            - <a:ext
              uri="{28A0092
                C50C-407E-
                A947-
                70E740481C1
              <a14:useL
                val='
              xmlns
            </a:ext>
          </a:extLst>
        </a:blip>
        <a:srcRect/>
        - <a:stretch>
          <a:fillRect/>
        </a:stretch>
      </pic:blipFill>
      - <pic:spPr bwMode="auto">
        - <a:xfrm>
          <a:off y="0"
            x="0"/>
          <a:ext
            cx="673100"
            cy="241300"/>
        </a:xfrm>

```

```

- <a:prstGeom
  prst="rect">
    <a:avLst/>
  </a:prstGeom>
  <a:noFill/>
- <a:ln
  <a:noFill/>
</a:ln>
</pic:spPr>
</pic:pic>
</a:graphicData>
</a:graphic>
</wp:inline>
</w:drawing>
</w:r>
</w:p>
</w:txbxContent>
</w:txbx>
- <wps:bodyPr anchorCtr="0" anchor="t" bIns="45720" rIns="91440"
  tIns="45720" lIns="91440" wrap="none" vert="horz" rot="0">
  <a:spAutoFit/>
</wps:bodyPr>
</wps:wsp>
</a:graphicData>
</a:graphic>
- <wp14:sizeRelH relativeFrom="margin">
  <wp14:pctWidth>0</wp14:pctWidth>
</wp14:sizeRelH>
- <wp14:sizeRelV relativeFrom="margin">
  <wp14:pctHeight>0</wp14:pctHeight>
</wp14:sizeRelV>
</wp:anchor>
</w:drawing>
</mc:Choice>
- <mc:Fallback>
  - <w:pict>
    - <v:shape id="_x0000_s1037" w14:anchorId="46B71390" stroked="f"
      o:gfxdata="UESDBBQABgAIAAAAIQC2gziS/gAAAOEBAAATAAAAW0NvbnRlbnRfV
      90jcwflWJU67QAgI6YK0S0CoHGBkTxKLZGx5TGhvJ5O2G0SRWNoz/78nu9wcxkFMJ
      0s5Y6ir5vt9lD1JwBDIwOMJKHpHlpr69KfdHjyxSmriSfYz+USnWPY7AufNIadK6MEJ
      OITrorhX2lFEilmcO2RdNtjC5xDF9pCuTyYBB5bi6bQ4syoJ3g9WQ0ymailZg5KdCXIK
      SUOqXwnz5DrgnHtJTxOsQfEKIT7DmDSUCaxw7Rqn8787ZsmRM9e2VmPeBN4uqYv
      JsXecLq0q+WD6m8AAD//wMAUESDBBQABgAIAAAAIQA4/SH/1gAAAJQBAAALAA
      bHOKkMFqWzAMhu+DvYPRfXGawxijTi+j0GvpHsDYimMaW0Yy2fr2M4PBMnrUb/
      JVI2sOt6UJgd+ZiDgffL8ekFIFSBvV0oo4EbChzGx4f9GRdb25HMsYhqlCwG5lrLq9biZl
      22YiTra2kYMu1lItQD30/bPm3wwYN0x18gb45AdQl1tp5j/sFB2T0FQ7R0nTNEV3j6o9f
      OWA14Fm+Q8a1a8+Bvu/d/dMb2JY5uiPbhG/ktn4cqGU/er3pcvwCAAD//wMAUESDBB
      IQD8viexHgIAAB8EAAAOAAAZHJzL2Uyb0RvYy54bWysU8G02yAQvVfqPyDujR3
      dttKu/0AjHGMCGgwCNnb69R1wkkbbW1UOiGGGx5s3M+vbUStyEM5LMDWdz3JKhC
      SnxgpmUKjKjpUXh6u3n7Zj3YShTQg2qFtwhifDXymvYh2CrLPO+FZn4GVhh0duA0C
      VlmR58tsANdaB1x4j7f3k5NuEn7XCR6+dZ0XgaiaIreQdpf2Ju7ZzS2qvWO2l/xEG/0DC8
      UPcsMPLi5F9QWnIHHrow46Az6DrJRcoBs5nnr7J56pkVKRcUx9uLTP7/wfKvh++OyL
      sxgD+QgjKa16g/UVBj1ZDAsjXmOVU6bePgD/6YmBbc/MXtw5B0MvW1vs5vFldvV0wv/
      2EuABDR2TkfpUAYC6Fi46UykQrHy5vl+2W0Ho6uYIGUZekWser82DofPgvQJB5q6r
      zFh1Dol/eVCy3UmlkuH2zVY5cmDYJLu0Ev9XYcqQoaarRbFIyAbi+9Q/WgZsYiUEs3
      tCkkMKmmMzJR5qROFGSSJozNmMqwOoveQHTeURxMPYszhoce3C9KbuzXmhocK
      GeXiQ4GGu/Y01x5mOALVNFAYHbchjUQSw95hYXYyirYrOPE4EcYuTFqeJia2+bW
      70i8g7VI3FqnpPQnzaZCICQQUqWWPoBjb5OIeB1itwlvj3uC42hGM9/k29G24kK9bxw
      TMMVwvHzdbLC4Ynio1rHhPBDHrF7U2uMuMG3tPIECORs9hnCqEOocuk9Lomq/z/
      X0nTqyGW21Y+JMICWtVwXKhVR8816a/D2SK8NH35rV36tlh+rrPVu70/D+04i3+NTx
      fKSHIjKV7szGixZh8rimsYt5fAbi6qdJCqJEWKVrkeUu/x8ofgEAAAP//AwBQSwECLQ
      ACEAtoM4kv4AAADhAQAAEwAAAAAAAAAAAAAAAAAAAAAAAAAAW0NvbnRlbnRfV
      ABQABgAIAAAAIQA4/SH/1gAAAJQBAAALAAAAAAAAAAAAAAAAAAC8BAABfcm
      ABQABgAIAAAAIQD8viexHgIAAB8EAAAOAAAAAAAAAAAAAAAAAAC4CAABkcn
      AQItABQABgAIAAAAIQBT2kPa3wAAAAgBAAAPAAAAAAAAAAAAAAAAAAAHgEA
      bWxQSwUGAAAAAAQABADzAAAAhAUAAAAA" style="position:absolute;margin-
      left:-2.85pt;margin-
      top:22.05pt;width:68pt;height:19.9pt;z-index:251705344;visibility:visible;mso-wrap-
      style:none;mso-width-percent:0;mso-height-percent:0;mso-wrap-distance-left:9pt;mso-
      wrap-distance-top:3.6pt;mso-wrap-distance-right:9pt;mso-wrap-distance-
      bottom:3.6pt;mso-position-horizontal:absolute;mso-position-horizontal-
      relative:margin;mso-position-vertical:absolute;mso-position-vertical-relative:text;mso-
      width-percent:0;mso-height-percent:0;mso-width-relative:margin;mso-height-
      relative:margin;v-text-anchor:top" type="#_x0000_t202">
      - <v:textbox style="mso-fit-shape-to-text:t">
        - <w:txbxContent>
          - <w:p w:rsidP="002D35A0" w:rsidRDefault="00F806F5"
            w:rsidR="00F806F5" w14:textId="77777777" w14:paraId="574528B8"
            w:rsidRPr="00847784">
            - <w:pPr>
              <w:spacing w:lineRule="auto" w:line="240" w:after="0"
                w:before="0"/>

```

```

        <w:ind w:left="11" w:hanging="11"/>
        <w:jc w:val="right"/>
        - <w:rPr>
            <w:lang w:val="fr-FR"/>
        </w:rPr>
    </w:pPr>
    - <w:r>
        - <w:rPr>
            <w:noProof/>
        </w:rPr>
        - <w:drawing>
            - <wp:inline wp14:editId="1D4CC746"
              wp14:anchorId="4C4C119E" distR="0" distL="0" distB="0"
              distT="0">
                <wp:extent cx="673100" cy="241300"/>
                <wp:effectExtent r="0" b="6350" t="0" l="0"/>
                <wp:docPr name="Picture 11" id="11"/>
                - <wp:cNvGraphicFramePr>
                    <a:graphicFrameLocks noChangeAspect="1"
                      xmlns:a="http://schemas.openxmlformats.org/d
                    </wp:cNvGraphicFramePr>
                - <a:graphic
                  xmlns:a="http://schemas.openxmlformats.org/drawingml
                - <a:graphicData
                  uri="http://schemas.openxmlformats.org/drawingml
                - <pic:pic
                  xmlns:pic="http://schemas.openxmlformats.org
                - <pic:nvPicPr>
                    <pic:cNvPr name="Picture 1"
                      id="0"/>
                - <pic:cNvPicPr>
                    <a:picLocks noChangeAspect="1"
                      noChangeArrowheads="1"/>
                </pic:cNvPicPr>
                </pic:nvPicPr>
                - <pic:blipFill>
                    - <a:blip r:embed="rId14">
                        - <a:extLst>
                            - <a:ext uri="{28A0092B-
                              C50C-407E-A947-
                              70E740481C1C}">
                                <a14:useLocalDpi
                                  val="0"
                                  xmlns:a14="http://s
                                </a:ext>
                            </a:extLst>
                        </a:blip>
                        <a:srcRect/>
                    - <a:stretch>
                        <a:fillRect/>
                    </a:stretch>
                </pic:blipFill>
                - <pic:spPr bwMode="auto">
                    - <a:xfrm>
                        <a:off y="0" x="0"/>
                        <a:ext cx="673100"
                          cy="241300"/>
                    </a:xfrm>
                    - <a:prstGeom prst="rect">
                        <a:avLst/>
                        </a:prstGeom>
                        <a:noFill/>
                    - <a:ln>
                        <a:noFill/>
                    </a:ln>
                </pic:spPr>
            </pic:pic>
        </a:graphicData>
    </a:graphic>
</wp:inline>
</w:drawing>
</w:r>
</w:p>
</w:txbxContent>
</v:textbox>
<w10:wrap anchorx="margin"/>
</v:shape>
</w:pict>
</mc:Fallback>
</mc:AlternateContent>
</w:r>
- <w:hyperlink r:id="rId15" w:history="1">

```

```

- <w:r w:rsidRPr="005C028C">
  - <w:rPr>
    <w:rStyle w:val="Hyperlink"/>
    <w:rFonts w:hAnsi="Tw Cen MT" w:ascii="Tw Cen MT"/>
    <w:sz w:val="18"/>
    <w:szCs w:val="18"/>
  </w:rPr>
  <w:t>www.najfnr.or</w:t>
</w:r>
</w:hyperlink>
- <w:r w:rsidRPr="005C028C">
  - <w:rPr>
    <w:rStyle w:val="Hyperlink"/>
    <w:rFonts w:hAnsi="Tw Cen MT" w:ascii="Tw Cen MT"/>
    <w:sz w:val="18"/>
    <w:szCs w:val="18"/>
  </w:rPr>
  <w:t>g</w:t>
</w:r>
</w:p>
</w:tc>
</w:tr>
- <w:tr w:rsidR="002D35A0" w14:textId="77777777" w14:paraId="3D3F9229" w:rsidRPr="005C028C" w:rsidTr="0099201C">
  - <w:trPr>
    <w:trHeight w:val="1013"/>
  </w:trPr>
  - <w:tc>
    - <w:tcPr>
      <w:tcW w:w="1615" w:type="dxa"/>
    </w:tcPr>
    - <w:p w:rsidP="00033A39" w:rsidRDefault="002D35A0" w:rsidR="002D35A0" w14:textId="77777777" w14:paraId="7A5EF33E" w:rsidRPr="005C028C">
      - <w:pPr>
        <w:spacing w:lineRule="auto" w:line="259" w:after="0" w:before="0"/>
        <w:ind w:right="0" w:left="0" w:firstLine="0"/>
        <w:jc w:val="center"/>
      </w:pPr>
      - <w:rPr>
        <w:rFonts w:hAnsi="Tw Cen MT" w:ascii="Tw Cen MT"/>
      </w:rPr>
    </w:p>
  </w:tc>
  - <w:r w:rsidRPr="005C028C">
    - <w:rPr>
      <w:noProof/>
    </w:rPr>
  </w:tc>
- <w:drawing>
  - <wp:anchor wp14:editId="2E8BCF76" wp14:anchorId="6D09DDB8" allowOverlap="1" layoutInCell="1" locked="0" behindDoc="0" relativeHeight="251704320" simplePos="0" distR="114300" distL="114300" distB="0" distT="0">
    <wp:simplePos y="0" x="0"/>
    - <wp:positionH relativeFrom="column">
      <wp:posOffset>207678</wp:posOffset>
    </wp:positionH>
    - <wp:positionV relativeFrom="paragraph">
      <wp:posOffset>90203</wp:posOffset>
    </wp:positionV>
    <wp:extent cx="486888" cy="457200"/>
    <wp:effectExtent r="8890" b="0" t="0" l="0"/>
    <wp:wrapNone/>
    <wp:docPr name="Picture 1" id="1"/>
  </wp:cNvGraphicFramePr>
  <a:graphicFrameLocks noChangeAspect="1" xmlns:a="http://schemas.openxmlformats.org/drawingml/2006/main"/>
</wp:cNvGraphicFramePr>
- <a:graphic xmlns:a="http://schemas.openxmlformats.org/drawingml/2006/main">
  - <a:graphicData uri="http://schemas.openxmlformats.org/drawingml/2006/picture">
    - <pic:pic xmlns:pic="http://schemas.openxmlformats.org/drawingml/2006/picture">
      - <pic:nvPicPr>
        <pic:cNvPr name="" id="1"/>
        <pic:cNvPicPr>
          <pic:nvPicPr>
            <pic:blipFill>
              - <a:blip cstate="print" r:embed="rId16">
                - <a:extLst>
                  - <a:ext uri="{28A0092B-C50C-407E-A947-70E740481C1C}">
                    <a14:useLocalDpi val="0" xmlns:a14="http://schemas.microsoft.com/office/drawing" />
                  </a:ext>
                </a:extLst>
              </a:blip>
            - <a:stretch>
              <a:fillRect/>
            </a:stretch>
          </pic:blipFill>
        </pic:nvPicPr>
      </pic:pic>
    </a:graphicData>
  </a:graphic>

```

```

        </pic:blipFill>
        - <pic:spPr>
            - <a:xfmr>
                <a:off y="0" x="0"/>
                <a:ext cx="486888" cy="457200"/>
            </a:xfmr>
            - <a:prstGeom prst="rect">
                <a:avLst/>
            </a:prstGeom>
        </pic:spPr>
    </pic:pic>
    <a:graphicData>
        </a:graphic>
        - <wp14:sizeRelH relativeFrom="margin">
            <wp14:pctWidth>0</wp14:pctWidth>
        </wp14:sizeRelH>
        - <wp14:sizeRelV relativeFrom="margin">
            <wp14:pctHeight>0</wp14:pctHeight>
        </wp14:sizeRelV>
    </wp:anchor>
</w:drawing>
</w:r>
</w:p>
</w:tc>
- <w:tc>
    - <w:tcPr>
        <w:tcW w:w="1620" w:type="dxa"/>
        <w:vMerge/>
    </w:tcPr>
    - <w:p w:rsidP="00033A39" w:rsidRDefault="002D35A0" w:rsidR="002D35A0" w14:textId="77777777"
        w14:paraId="27A698C5" w:rsidRPr="005C028C">
        - <w:pPr>
            <w:spacing w:lineRule="auto" w:line="259" w:after="0" w:before="0"/>
            <w:ind w:right="0" w:left="0" w:firstLine="0"/>
            <w:jc w:val="left"/>
        - <w:rPr>
            <w:rFonts w:hAnsi="Tw Cen MT" w:ascii="Tw Cen MT"/>
        </w:rPr>
    </w:pPr>
</w:p>
</w:tc>
</w:tr>
- <w:tr w:rsidR="002D35A0" w14:textId="77777777" w14:paraId="36E1412F" w:rsidRPr="005C028C" w:rsidTr="0099201C">
    - <w:trPr>
        <w:trHeight w:val="202"/>
    </w:trPr>
    - <w:tc>
        - <w:tcPr>
            <w:tcW w:w="3235" w:type="dxa"/>
            <w:gridSpan w:val="2"/>
        </w:tcPr>
        - <w:p w:rsidP="00033A39" w:rsidRDefault="001E1E05" w:rsidR="002D35A0" w14:textId="0BA47E01"
            w14:paraId="4AD70B81" w:rsidRPr="00CD7A6F">
            - <w:pPr>
                <w:spacing w:lineRule="auto" w:line="259" w:after="0" w:before="0"/>
                <w:ind w:right="0" w:left="235"/>
                <w:jc w:val="center"/>
            - <w:rPr>
                <w:rFonts w:hAnsi="Arial Black" w:ascii="Arial Black"/>
                <w:b/>
                <w:color w:val="385623" w:themeShade="80" w:themeColor="accent6"/>
                <w:spacing w:val="20"/>
                <w:sz w:val="12"/>
                <w:szCs w:val="12"/>
            </w:rPr>
        </w:pPr>
        - <w:r w:rsidRPr="001E1E05">
            - <w:rPr>
                <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight"
                    w:ascii="Leelawadee UI Semilight" w:eastAsia="Leelawadee UI Semilight"/>
                <w:color w:val="0563C1"/>
                <w:sz w:val="12"/>
                <w:szCs w:val="12"/>
                <w:u w:val="single" w:color="0563C1"/>
            </w:rPr>
            <w:t>https://doi.org/</w:t>
        </w:r>
        - <w:r w:rsidR="007A215C" w:rsidRPr="007A215C">
            - <w:rPr>
                <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight"
                    w:ascii="Leelawadee UI Semilight" w:eastAsia="Leelawadee UI Semilight"/>
                <w:color w:val="0563C1"/>
            </w:rPr>

```

```

        <w:sz w:val="12"/>
        <w:szCs w:val="12"/>
        <w:u w:val="single" w:color="0563C1"/>
        </w:rPr>
        <w:t>10.5281/zenodo.2575438</w:t>
        </w:r>
        </w:p>
        </w:tc>
        </w:tr>
        </w:tbl>
        - <w:p w:rsidP="00033A39" w:rsidRDefault="00C62C26" w:rsidR="00C62C26" w14:textId="77777777" w14:paraId="7A8E826F">
            - <w:pPr>
                <w:spacing w:lineRule="auto" w:line="259" w:after="120" w:before="0"/>
                <w:ind w:right="0" w:left="0" w:firstLine="0"/>
                <w:jc w:val="left"/>
                - <w:rPr>
                    <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI Semilight"/>
                    <w:sz w:val="14"/>
                    <w:szCs w:val="14"/>
                </w:rPr>
            </w:pPr>
        </w:p>
        - <w:p w:rsidP="00033A39" w:rsidRDefault="00C62C26" w:rsidR="00C62C26" w14:textId="77777777" w14:paraId="482EDEC6">
            - <w:pPr>
                <w:spacing w:lineRule="auto" w:line="259" w:after="5" w:before="0"/>
                <w:ind w:right="0" w:left="0" w:firstLine="0"/>
                - <w:rPr>
                    <w:rFonts w:hAnsi="Tw Cen MT" w:ascii="Tw Cen MT"/>
                    <w:color w:val="000000" w:themeColor="text1"/>
                    <w:sz w:val="18"/>
                    <w:szCs w:val="18"/>
                </w:rPr>
            </w:pPr>
        </w:p>
        </w:tc>
        - <w:tc>
            - <w:tcPr>
                <w:tcW w:w="5789" w:type="dxa"/>
            </w:tcPr>
            - <w:p w:rsidP="00033A39" w:rsidRDefault="00C62C26" w:rsidR="00C62C26" w14:textId="77777777" w14:paraId="492534E9" w:rsidRPr="009D4F1E">
                - <w:pPr>
                    <w:spacing w:lineRule="auto" w:line="240" w:after="0" w:before="0"/>
                    <w:ind w:right="0" w:left="-14" w:firstLine="0"/>
                    - <w:rPr>
                        <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI Semilight"/>
                        <w:color w:val="auto"/>
                        <w:sz w:val="15"/>
                        <w:szCs w:val="15"/>
                    </w:rPr>
                </w:pPr>
                - <w:r w:rsidRPr="009D4F1E">
                    - <w:rPr>
                        <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI Semilight"/>
                        <w:b/>
                        <w:bCs/>
                        <w:color w:val="auto"/>
                        <w:sz w:val="15"/>
                        <w:szCs w:val="15"/>
                    </w:rPr>
                        <w:t xml:space="preserve">Background:</w:t>
                    </w:r>
                - <w:r w:rsidR="00E84991" w:rsidRPr="009D4F1E">
                    - <w:rPr>
                        <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI Semilight"/>
                        <w:color w:val="auto"/>
                        <w:sz w:val="15"/>
                        <w:szCs w:val="15"/>
                    </w:rPr>
                        <w:t>C</w:t>
                    </w:r>
                - <w:r w:rsidR="009734FE" w:rsidRPr="009D4F1E">
                    - <w:rPr>
                        <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI Semilight"/>
                        <w:color w:val="auto"/>
                        <w:sz w:val="15"/>
                        <w:szCs w:val="15"/>
                    </w:rPr>

```



```

        </w:rPr>
        <w:t>arotenoids have been hypothesized to promote the prevention and treatment of prostate cancer (PC).</w:t>
    </w:r>
    - <w:r w:rsidRPr="009D4F1E">
        - <w:rPr>
            <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI
            Semilight"/>
            <w:color w:val="auto"/>
            <w:sz w:val="15"/>
            <w:szCs w:val="15"/>
        </w:rPr>
        <w:t xml:space="preserve"></w:t>
    </w:r>
    - <w:r w:rsidRPr="009D4F1E">
        - <w:rPr>
            <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI
            Semilight"/>
            <w:b/>
            <w:bCs/>
            <w:color w:val="auto"/>
            <w:sz w:val="15"/>
            <w:szCs w:val="15"/>
        </w:rPr>
        <w:t xml:space="preserve">Aims: </w:t>
    </w:r>
    - <w:r w:rsidR="009734FE" w:rsidRPr="009D4F1E">
        - <w:rPr>
            <w:color w:val="auto"/>
            <w:sz w:val="15"/>
            <w:szCs w:val="15"/>
        </w:rPr>
        <w:t xml:space="preserve"></w:t>
    </w:r>
    - <w:r w:rsidR="009734FE" w:rsidRPr="009D4F1E">
        - <w:rPr>
            <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI
            Semilight"/>
            <w:color w:val="auto"/>
            <w:sz w:val="15"/>
            <w:szCs w:val="15"/>
        </w:rPr>
        <w:t xml:space="preserve">Conducting a meta-analysis to </w:t>
    </w:r>
    - <w:r w:rsidR="00567B6B" w:rsidRPr="009D4F1E">
        - <w:rPr>
            <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI
            Semilight"/>
            <w:color w:val="auto"/>
            <w:sz w:val="15"/>
            <w:szCs w:val="15"/>
        </w:rPr>
        <w:t>assess</w:t>
    </w:r>
    - <w:r w:rsidR="009734FE" w:rsidRPr="009D4F1E">
        - <w:rPr>
            <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI
            Semilight"/>
            <w:color w:val="auto"/>
            <w:sz w:val="15"/>
            <w:szCs w:val="15"/>
        </w:rPr>
        <w:t xml:space="preserve"> whether the association differs by the type of carotenoids and to compare the relationships of
        each type of carotenoid with PC risk.</w:t>
    </w:r>
    - <w:r w:rsidR="00B85133" w:rsidRPr="009D4F1E">
        - <w:rPr>
            <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI
            Semilight"/>
            <w:color w:val="auto"/>
            <w:sz w:val="15"/>
            <w:szCs w:val="15"/>
        </w:rPr>
        <w:t xml:space="preserve"></w:t>
    </w:r>
    - <w:r w:rsidRPr="009D4F1E">
        - <w:rPr>
            <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI
            Semilight"/>
            <w:b/>
            <w:bCs/>
            <w:color w:val="auto"/>
            <w:sz w:val="15"/>

```

```

        <w:szCs w:val="15"/>
        </w:rPr>
        <w:t xml:space="preserve">Methods and Material: </w:t>
    </w:r>
    - <w:r w:rsidR="00B85133" w:rsidRPr="009D4F1E">
        - <w:rPr>
            <w:color w:val="auto"/>
            <w:sz w:val="15"/>
            <w:szCs w:val="15"/>
        </w:rPr>
        <w:t xml:space="preserve"> </w:t>
    </w:r>
    - <w:r w:rsidR="00B85133" w:rsidRPr="009D4F1E">
        - <w:rPr>
            <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI
            Semilight"/>
            <w:color w:val="auto"/>
            <w:sz w:val="15"/>
            <w:szCs w:val="15"/>
        </w:rPr>
        <w:t>A literature search was conducted using the PubMed database. Pertinent studies were included in the meta-analysis of
        higher versus lower categories of dietary intakes or serum concentrations of carotenoids in relation to PC. A random-
        effects model was used to obtain the pooled odds ratios (ORs) and their confidence intervals (95%) of the case-control
        and cohort studies, for generic inverse variance data.</w:t>
    </w:r>
    - <w:r w:rsidRPr="009D4F1E">
        - <w:rPr>
            <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI
            Semilight"/>
            <w:b/>
            <w:bCs/>
            <w:color w:val="auto"/>
            <w:sz w:val="15"/>
            <w:szCs w:val="15"/>
        </w:rPr>
        <w:t xml:space="preserve">Results: </w:t>
    </w:r>
    - <w:r w:rsidR="009D36E0" w:rsidRPr="009D4F1E">
        - <w:rPr>
            <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI
            Semilight"/>
            <w:color w:val="auto"/>
            <w:sz w:val="15"/>
            <w:szCs w:val="15"/>
        </w:rPr>
        <w:t xml:space="preserve">13 </w:t>
    </w:r>
    - <w:r w:rsidR="00567B6B" w:rsidRPr="009D4F1E">
        - <w:rPr>
            <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI
            Semilight"/>
            <w:color w:val="auto"/>
            <w:sz w:val="15"/>
            <w:szCs w:val="15"/>
        </w:rPr>
        <w:t xml:space="preserve">identified </w:t>
    </w:r>
    - <w:r w:rsidR="009D36E0" w:rsidRPr="009D4F1E">
        - <w:rPr>
            <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI
            Semilight"/>
            <w:color w:val="auto"/>
            <w:sz w:val="15"/>
            <w:szCs w:val="15"/>
        </w:rPr>
        <w:t>studies involved 44,861 participants. The meta-analysis determined, for total carotenoids and lycopene, a statistically
        significant relationship with PC risk</w:t>
    </w:r>
    - <w:r w:rsidR="00FA529C" w:rsidRPr="009D4F1E">
        - <w:rPr>
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            Semilight"/>
            <w:color w:val="auto"/>
            <w:sz w:val="15"/>
            <w:szCs w:val="15"/>
        </w:rPr>
        <w:t></w:t>
    </w:r>
    - <w:r w:rsidR="009D36E0" w:rsidRPr="009D4F1E">
        - <w:rPr>
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            Semilight"/>

```

```

        <w:color w:val="auto"/>
        <w:sz w:val="15"/>
        <w:szCs w:val="15"/>
    </w:rPr>
    <w:t xml:space="preserve"> OR</w:t>
</w:r>
- <w:r w:rsidR="00FA529C" w:rsidRPr="009D4F1E">
    - <w:rPr>
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        Semilight"/>
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        <w:sz w:val="15"/>
        <w:szCs w:val="15"/>
    </w:rPr>
    <w:t></w:t>
</w:r>
- <w:r w:rsidR="009D36E0" w:rsidRPr="009D4F1E">
    - <w:rPr>
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        Semilight"/>
        <w:color w:val="auto"/>
        <w:sz w:val="15"/>
        <w:szCs w:val="15"/>
    </w:rPr>
    <w:t xml:space="preserve"> 0.88; 95% CI 0.81-0.96 and 0.87; 95% CI 0.77-0.99 respectively. However, no other
    carotenoid was noticed to have a statistically significant association with PC risk. Comparison of the effect of each type
    of carotenoid on PC risk showed that lycopene, lutein-zeaxanthin, and </w:t>
</w:r>
- <w:r w:rsidR="009D36E0" w:rsidRPr="009D4F1E">
    - <w:rPr>
        <w:color w:val="auto"/>
        <w:sz w:val="15"/>
        <w:szCs w:val="15"/>
    </w:rPr>
    <w:t> $\beta$ </w:t>
</w:r>
- <w:r w:rsidR="009D36E0" w:rsidRPr="009D4F1E">
    - <w:rPr>
        <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI
        Semilight"/>
        <w:color w:val="auto"/>
        <w:sz w:val="15"/>
        <w:szCs w:val="15"/>
    </w:rPr>
    <w:t xml:space="preserve">-cryptoxanthin had a moderate inverse but not statistically significant relationship with PC risk.
    Compared to </w:t>
</w:r>
- <w:r w:rsidR="009D36E0" w:rsidRPr="009D4F1E">
    - <w:rPr>
        <w:color w:val="auto"/>
        <w:sz w:val="15"/>
        <w:szCs w:val="15"/>
    </w:rPr>
    <w:t> $\beta$ </w:t>
</w:r>
- <w:r w:rsidR="009D36E0" w:rsidRPr="009D4F1E">
    - <w:rPr>
        <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI
        Semilight"/>
        <w:color w:val="auto"/>
        <w:sz w:val="15"/>
        <w:szCs w:val="15"/>
    </w:rPr>
    <w:t xml:space="preserve">-carotene, and </w:t>
</w:r>
- <w:r w:rsidR="009D36E0" w:rsidRPr="009D4F1E">
    - <w:rPr>
        <w:color w:val="auto"/>
        <w:sz w:val="15"/>
        <w:szCs w:val="15"/>
    </w:rPr>
    <w:t> $\alpha$ </w:t>
</w:r>
- <w:r w:rsidR="009D36E0" w:rsidRPr="009D4F1E">
    - <w:rPr>
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        Semilight"/>
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        <w:sz w:val="15"/>
        <w:szCs w:val="15"/>
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    <w:t>-carotene results, their effect estimates were higher than the previous carotenoids.</w:t>

```

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  - <w:rPr>
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    <w:sz w:val="15"/>
    <w:szCs w:val="15"/>
  </w:rPr>
  <w:t xml:space="preserve"></w:t>
</w:r>
- <w:r w:rsidRPr="009D4F1E">
  - <w:rPr>
    <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI Semilight"/>
    <w:b/>
    <w:bCs/>
    <w:color w:val="auto"/>
    <w:sz w:val="15"/>
    <w:szCs w:val="15"/>
  </w:rPr>
  <w:t xml:space="preserve">Conclusions: </w:t>
</w:r>
- <w:r w:rsidR="009D36E0" w:rsidRPr="009D4F1E">
  - <w:rPr>
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  </w:rPr>
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- <w:r w:rsidR="009D36E0" w:rsidRPr="009D4F1E">
  - <w:rPr>
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    <w:color w:val="auto"/>
    <w:sz w:val="15"/>
    <w:szCs w:val="15"/>
  </w:rPr>
  <w:t>Our findings indicate that PC was inversely associated with total carotenoids and lycopene dietary intake and serum concentrations. These data provide support for the utilization of carotenoids for the treatment and prevention of PC.</w:t>
</w:r>
</w:p>
- <w:p w:rsidP="00151143" w:rsidRDefault="00695689" w:rsidR="00C62C26" w14:textId="77777777" w14:paraId="336BA676" w:rsidRPr="00B85133">
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  - <w:rPr>
    <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI Semilight"/>
    <w:color w:val="auto"/>
    <w:sz w:val="15"/>
    <w:szCs w:val="15"/>
  </w:rPr>
</w:pPr>
- <w:r w:rsidRPr="00B85133">
  - <w:rPr>
    <w:rFonts w:hAnsi="Tw Cen MT" w:ascii="Tw Cen MT"/>
    <w:i/>
    <w:iCs/>
    <w:noProof/>
    <w:color w:val="538135" w:themeShade="BF" w:themeColor="accent6"/>
    <w:sz w:val="15"/>
    <w:szCs w:val="15"/>
  </w:rPr>
  <w:t xml:space="preserve">Article edited </w:t>
</w:r>
- <w:r w:rsidR="002D35A0" w:rsidRPr="00B85133">
  - <w:rPr>
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    <w:sz w:val="15"/>
    <w:szCs w:val="15"/>
  </w:rPr>
  <w:t>by</w:t>
</w:r>
- <w:r w:rsidR="005710A1">
  - <w:rPr>
    <w:rFonts w:hAnsi="Tw Cen MT" w:ascii="Tw Cen MT"/>

```

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        <w:szCs w:val="15"/>
    </w:rPr>
    <w:t xml:space="preserve"> Pr. Meghit Boumediene KHALED and</w:t>
</w:r>
- <w:r w:rsidR="00151143">
    - <w:rPr>
        <w:rFonts w:hAnsi="Tw Cen MT" w:ascii="Tw Cen MT"/>
        <w:i/>
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        <w:sz w:val="15"/>
        <w:szCs w:val="15"/>
    </w:rPr>
    <w:t xml:space="preserve"> Dr.</w:t>
</w:r>
- <w:r w:rsidR="00F51D56">
    <w:t xml:space="preserve"> </w:t>
</w:r>
<w:proofErr w:type="spellStart"/>
- <w:r w:rsidR="00F51D56" w:rsidRPr="00F51D56">
    - <w:rPr>
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    </w:rPr>
    <w:t>Mickaël</w:t>
</w:r>
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    - <w:rPr>
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        <w:i/>
        <w:iCs/>
        <w:color w:val="538135" w:themeShade="BF" w:themeColor="accent6"/>
        <w:sz w:val="15"/>
        <w:szCs w:val="15"/>
    </w:rPr>
    <w:t xml:space="preserve"> RIALLAND</w:t>
</w:r>
</w:p>
</w:tc>
</w:tr>
</w:tbl>
- <w:p w:rsidP="00C62C26" w:rsidRDefault="00C62C26" w:rsidR="00C62C26" w14:textId="77777777" w14:paraId="2FD63730">
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        <w:ind w:right="0" w:left="235"/>
    - <w:rPr>
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        <w:color w:val="385623" w:themeShade="80" w:themeColor="accent6"/>
        <w:sz w:val="16"/>
        <w:szCs w:val="16"/>
    </w:rPr>
</w:pPr>
</w:p>
- <w:p w:rsidP="00C62C26" w:rsidRDefault="00C62C26" w:rsidR="00C62C26" w14:textId="77777777" w14:paraId="480FF08C">
    - <w:pPr>
        <w:spacing w:lineRule="auto" w:line="259" w:after="5" w:before="0"/>
        <w:ind w:right="0" w:left="235"/>
    - <w:rPr>
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        <w:sz w:val="16"/>
        <w:szCs w:val="16"/>
    </w:rPr>
</w:pPr>
</w:p>
- <w:p w:rsidP="00C62C26" w:rsidRDefault="00C62C26" w:rsidR="00C62C26" w14:textId="77777777" w14:paraId="268C08F9">
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        <w:ind w:right="0" w:left="235"/>
    - <w:rPr>
        <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI Semilight"/>
        <w:color w:val="385623" w:themeShade="80" w:themeColor="accent6"/>

```

```

        <w:sz w:val="16"/>
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    </w:pPr>
  </w:p>
  - <w:p w:rsidP="00C62C26" w:rsidRDefault="00C62C26" w:rsidR="00C62C26" w14:textId="77777777" w14:paraId="6540F153">
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      <w:ind w:right="0" w:left="235"/>
      - <w:rPr>
        <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI Semilight"/>
        <w:color w:val="385623" w:themeShade="80" w:themeColor="accent6"/>
        <w:sz w:val="16"/>
        <w:szCs w:val="16"/>
      </w:rPr>
    </w:pPr>
  </w:p>
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        <w:rFonts w:cs="Leelawadee UI Semilight" w:hAnsi="Leelawadee UI Semilight" w:ascii="Leelawadee UI Semilight"/>
        <w:color w:val="385623" w:themeShade="80" w:themeColor="accent6"/>
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        <w:szCs w:val="16"/>
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    </w:pPr>
  - <w:r w:rsidRPr="005C028C">
    - <w:rPr>
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      <w:szCs w:val="18"/>
    </w:rPr>
  - <mc:AlternateContent>
    - <mc:Choice Requires="wpg">
      - <w:drawing>
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            <wp:posOffset>48260</wp:posOffset>
          </wp:positionH>
          - <wp:positionV relativeFrom="paragraph">
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          </wp:positionV>
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          <wp:docPr name="Group 10992" id="10992"/>
          <wp:cNvGraphicFramePr>
            - <a:graphic xmlns:a="http://schemas.openxmlformats.org/drawingml/2006/main">
              - <a:graphicData uri="http://schemas.microsoft.com/office/word/2010/wordprocessingGroup">
                - <wpg:wpg>
                  <wpg:cNvGrpSpPr>
                    - <wpg:grpSpPr>
                      - <a:xfrm>
                        <a:off y="0" x="0"/>
                        <a:ext cx="5981065" cy="12065"/>
                        <a:chOff y="0" x="0"/>
                        <a:chExt cx="5981389" cy="12192"/>
                      </a:xfrm>
                    </wpg:grpSpPr>
                  - <wps:wsp>
                    <wps:cNvPr name="Shape 13837" id="13837"/>
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                      - <wps:spPr>
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                      - <a:custGeom>
                        <a:avLst>
                          <a:gdLst>
                            <a:ahLst>
                              <a:cxnLst>
                                <a:rect r="0" b="0" t="0" l="0"/>
                              </a:cxnLst>
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                                - <a:path w="2085082" h="12192">
                                  - <a:moveTo>
                                    <a:pt y="0" x="0"/>

```

```

        </a:moveTo>
      - <a:lnTo>
        <a:pt y="0" x="2085082"/>
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      - <a:lnTo>
        <a:pt y="12192" x="2085082"/>
      </a:lnTo>
      - <a:lnTo>
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      - <a:lnTo>
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      </a:lnTo>
    </a:path>
  </a:pathLst>
  <a:custGeom>
  - <a:solidFill>
    <a:schemeClr val="accent6"/>
    <a:solidFill>
    - <a:ln w="0" cap="flat">
      <a:miter lim="127000"/>
    </a:ln>
  </wps:spPr>
  - <wps:style>
    - <a:lnRef idx="0">
      - <a:srgbClr val="000000">
        <a:alpha val="0"/>
      </a:srgbClr>
    </a:lnRef>
    - <a:fillRef idx="1">
      <a:srgbClr val="000000"/>
    </a:fillRef>
    - <a:effectRef idx="0">
      <a:scrgbClr r="0" b="0" g="0"/>
    </a:effectRef>
    <a:fontRef idx="none"/>
  </wps:style>
  <wps:bodyPr>
</wps:wsp>
- <wps:wsp>
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  - <wps:spPr>
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    </a:xfrm>
    - <a:custGeom>
      <a:avLst>
      <a:gdLst>
      <a:ahLst>
      <a:cxnLst>
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      - <a:pathLst>
        - <a:path w="3628003" h="12192">
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            <a:pt y="0" x="0"/>
          </a:moveTo>
          - <a:lnTo>
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          </a:lnTo>
          - <a:lnTo>
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          - <a:lnTo>
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      </a:pathLst>
    </a:custGeom>
    - <a:solidFill>
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      <a:solidFill>
      - <a:ln w="0" cap="flat">
        <a:miter lim="127000"/>
      </a:ln>
    </wps:spPr>
  - <wps:style>
    - <a:lnRef idx="0">

```

```

- <a:srgbClr val="000000">
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</a:srgbClr>
</a:lnRef>
- <a:fillRef idx="1">
  <a:srgbClr val="000000"/>
</a:fillRef>
- <a:effectRef idx="0">
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</a:effectRef>
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</wps:wsp>
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- <wp14:sizeRelV relativeFrom="margin">
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- <mc:Fallback>
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INTRODUCTION

Prostate cancer (PC) or carcinoma of the prostate is ranked as the second most common cancer within men worldwide [

1

]. An estimated number of 1.3 million cases were diagnosed worldwide with PC in 2018, accounting for 13.5 % of the cancers diagnosed in men, with almost 63 % of them (802

294) occurring in more developed regions [

2

]. The development of PC is complex and influenced by a combination of genetic, hormonal, and social factors. Carotenoids represent biologically active phytochemicals which are present as micro-components in fruits and vegetables and are responsible for their yellow, orange and red colors [

3

]. These micronutrients are thought to be responsible for the beneficial properties of fruits and vegetables in preventing human diseases including cardiovascular diseases [

4

], cancer [

5

-

7

]

, and other chronic diseases, and have distinct anti-oxidative properties, including protecting DNA and other important biomolecules from free radicals [

8

]. In recent years the antioxidant properties of carotenoids have been the major focus of research. More than 600 carotenoids have so far been identified in nature. However, only about 40 are present in a typical human diet.

Among these 40

, about 20 carotenoids have been identified in human blood and tissues. Close to 90% of the carotenoids

,

in

the

diet and

the

human body

,

is represented by alpha-carotene, beta-carotene, lutein, beta-cryptoxanthin

,

and lycopene

[

9

]. Higher consumption of tomato products, dietary lycopene intake, and circulating lycopene concentrations were

found to be inversely associated with prostate cancer risk [

10,11

].

Many epidemiological studies have investigated the association between prostate cancer and carotenoids, however, results have been inconsistent [

12,13

]. Consequently, In the current study, we aimed to investigate the relationship between dietary intake or blood concentrations of these carotenoids and their potential preventive effect on PC.

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345135

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MATERIAL AND METHODS

Search strategy

Th

e current

meta-analysis was performed in accordance with PRISMA guidelines

[

14

]. The literature search was independently undertaken by two authors (H.B and M.B). The author (S.E) made the final decision in case of any discrepancy. A comprehensive literature search was conducted using the PubMed database [

<https://www.ncbi.nlm.nih.gov/pubmed>

] to identify relevant English published articles on the relationship between carotenoids dietary intake or supplementation and the risk of PC. Using medical subject heading (Mesh), with the key terms: “carotenoids” and “prostatic neoplasms”. English full texts were searched with no population restriction (the final search was performed on 13 May 2018).

Study selection

Studies that met the following criteria were included in the meta-analysis: (a)

t

he study design was a cohort, and case-control

;

(b)
t
he primary outcome was clearly defined as prostate cancer
;
(c)
s
tudies that assessed the relationship between carotenoids (lycopene,
 β
-carotene,
 α
-carotene,
 β
-cryptoxanthin, and lutein/zeaxanthin) and PC risk
;
(d)
t
he exposure of interest was carotenoids intake and supplementation
;
(e)
t
he study provided Odds Ratios (OR) with 95% confidence intervals (CI) for exposure categories. Furthermore, letters, comments, and
articles
,
not published as full text, reviews, meta-analyses, animal studies, cellular culture, reports, and articles with missing or not appropriate
data
,
were excluded.
D
ata extraction
Data collection form
,
for each publication
,
was as follow: first author's name, year of publication, country of origin,
outcomes, recruitment and intervention periods, study type, number of cases, controls, total number, and age of participants in the
study, exposure values of carotenoids (serum and/or intake), and the adjusted confounders.
Summary measures
Review Manager 5.3 was utilized to analyze the data [
15
]. The pooled OR with 95% CI is given both for the fixed effects model and the random effects model. If value 1 is not within the 95%
CI, then the OR is statistically significant at the 5% level ($P \leq 0.05$) [
16
]. We used the study-specific OR for the highest versus lowest categories of dietary carotenoids intake or carotenoids concentration
exposure for the meta-analysis. The study selection, data extraction, and statistical analysis were independently undertaken by two
authors (H.B and M.B), a third author (S.E) made the final decision in case of any disagreement.
Publication bias
Publication bias and the small study effect were assessed using Begg's [
17
] rank correlation test and Egger's regression test [
18
], following a visual assessment of funnel plots. The R program was used
for
assessing
the bias risk across studies [
19
].
Sensitivity and subgroup analyses
Pre-Specified subgroup analyses were performed allowing for study types, location, methods used, and the adjusted confounders.
Furthermore, sensitivity analyses were performed by excluding one dataset at a time with the purpose of analyzing the influence of
each study on the effect estimates and the heterogeneity.
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359740
0
0
RESULTS
Study selection
The literature search yielded a total of 754 publications. After screening, 13 studies were included and 741 were excluded, among the
741 excluded articles, 470 did
n
o
t meet the criteria, 194 reviews, and meta-analysis, and 34 letters to editorial and comments, and 43 not appropriate or missing data
(Figure 1).
Study characteristics
Table 1 summarizes properties of the included studies. Two cohort and 11 case-control studies were included. Seven studies were
carried out in the USA [
12, 13, 20
-
24
], three in Australia [
25
-
27

],
t
wo
in Europe [
28, 29
, and one in Asia [
30
]. Among the included studies, eleven studies reported the effects of dietary intake or serum concentrations of lycopene and β -carotene on PC. With the exception of five studies, almost all adjusted analyses included age as a potential confounder and four studies controlled for family history of PC and body mass index (BMI).
Figure
SEQ Figure * ARABIC
1
:
Flowchart of study selection
R
elationship between carotenoids and risk of PC
The results of the meta-analysis
,
of highest versus lowest categories of carotenoids intake and serum concentrations
,
are summarized in table 2 and figure 2. A total of 44
. 861 participants from these studies were assigned to intervention or control groups. The number of participants in each case-control and cohort ranged from 321 to 29
. 361. The effects of lycopene and β -carotene were examined singly or in combination in six studies and in combination with other carotenoids in seven studies. The summary effect of the main analysis on PC was statistically significant with an OR of 0.88 (95% CI 0.81-0.96), with moderate heterogeneity ($I^2 = 56\%$). Thus, we conclude that carotenoids intake decreased the overall relative risk of PC. Nonetheless, we observed
,
after performing a sensitivity analysis
,
that one study (Jian
et al.
, 2004)
[
30
] constituted the major source of heterogeneity in our meta-analysis and after neglecting this study
,
I
2
dropped to only 2%.
Lycopene
A total of 11 studies with 15 datasets
,
on the relationship between lycopene and prostate cancer
,
were included. Our results showed that lycopene significantly reduced the prostate cancer risk (OR = 0.88; 95% CI 0.78-1.00), with moderate heterogeneity ($I^2 = 44\%$). According to further subgroup analysis
, as shown in Table 3, we did not identify significant associations between PC risk and lycopene for cohort studies ($P = 0.56$). However, case-control studies indicated that lycopene significantly decreased PC risk (OR = 0.87; 95% CI 0.77-0.99). Moreover, studies conducted in Australia and North American countries showed a stronger inverse relationship than European studies (OR = 0.76; 95% CI 0.53-1.09), (OR = 0.90; 95% CI 0.83-0.99, P (Z-test) = 0.03), and (OR = 0.94; 95% CI 0.75-1.16) respectively. Five studies with seven datasets reported data about dietary lycopene supplementation and PC risk. A statistically significant negative association was observed (OR = 0.83; 95% CI 0.70-0.99). A less strong and yet statistically non-significant inverse relationship was found between serum lycopene concentrations and PC (OR = 0.96; 95% CI 0.81-1.15).
 α
-Carotene
R
egarding the overall pooled estimates of the association between
 α
-carotene and PC risk, we noticed a statistically non-significant negative association with an OR of 0.80 (95% CI 0.60-1.07) and a moderate heterogeneity ($I^2 = 59\%$).
Alpha
carotene was found to decrease PC risk in case-control studies and in studies conducted in North American countries (OR = 0.86; 95% CI 0.64-1.15) and (OR = 0.87; 95% CI 0.59-1.29) respectively, although the associations were not statistically significant. The same pattern was noticed for studies investigating the effect of highest versus lowest categories of
 α
-carotene intake (OR = 0.87; 95% CI 0.59-1.29) and serum concentrations (OR = 0.65; 95% CI 0.33-1.27).

β
 -Carotene
 A total of 11 studies
 ,
 including 15 datasets
 ,
 reported data on
 β
 -carotene and PC risk. Comparing the highest with the lowest dietary intake or blood concentrations, a statistically non-significant inverse association was found with an OR of 0.95 (95% CI 0.78-1.11) and moderate heterogeneity ($I^2=54\%$). The main analysis was stratified according to study type, population, and methods used to assess the relationship. Therefore, nine studies with 13 datasets of case-control studies were pooled (OR = 0.95; 95% CI 0.78-1.16), and two cohort studies (OR = 0.79; 95% CI 0.46-1.35), suggesting a statistically non-significant negative association between
 β
 -carotene and PC risk. Our findings suggest that
 β
 -carotene has no effect on PC risk among North American (OR = 1.02; 95% CI 0.83-1.26), and Australian populations (OR = 1.00; 95% CI 0.76-1.31) and studies examining the effect of highest versus lowest categories of serum concentrations of
 β
 -carotene on PC (OR = 1.01; 95% CI 0.84-1.23).
 Table 1:
 Characteristics of included studies
 Case-control studies
 Adjusted confounders
 Age, administered vitamin A supplement
 .
 Age, study center, education, physical activity, body mass index, family history of prostate cancer and total calorie intake
 Age at specimen collection, fasting hours prior to blood draw, body mass index, family history of prostate cancer, and education
 .
 Exposure population, study center at randomization, age at randomization within 5-year intervals, sex, smoking status at randomization, and year of randomization.
 Age, locality, education, family income marital status, number of children, family history of prostate cancer, BMI, tea drinking, caloric intake, and fat intake.
 Social class
 .
 Age, height, total nonsteroidal anti-inflammatory drugs, and socioeconomic status
 .
 Age, time since initial screening, year of blood draw, and study center
 .
 Smoking, age, and randomized aspirin assignment
 .
 N/A
 Matching variables plus cholesterol levels, selenium supplementation, vitamin E supplementation, family history of prostate cancer, body mass index, height, vigorous exercise, history of vasectomy and current smoking
 .
 Cohort studies
 Adjusted confounders
 N/A
 N/A
 Type of carotenoids
 Lycopene
 Lycopene,
 β
 -carotene, Lutein
 Lycopene,
 β
 -carotene, Lutein,
 β
 -cryptoxanthin
 Lycopene,
 β
 -carotene,
 α
 -Carotene,
 β
 -Cryptoxanthin, Lutein
 Lycopene,
 β
 -carotene,
 α
 -carotene,
 β
 -cryptoxanthin, Lutein
 Lycopene
 Lycopene
 Lycopene,
 α
 -Carotene,
 β
 -Carotene,

β
 -Cryptoxanthin, Lutein
 β
 -carotene
 Lycopene
 β
 -carotene, Lycopene,
 β
 -cryptoxanthin, Lutein/zeaxanthin
 Type of carotenoids
 β
 -carotene, Lycopene,
 α
 -carotene
 β
 -carotene
 Methods
 Serum
 Dietary
 Serum
 Serum
 Dietary
 Dietary
 Dietary
 Serum
 Serum
 Dietary
 Serum
 Methods
 Serum
 Dietary
 Cases / controls
 96/225
 1294/1451
 467/936
 205/205
 130/274
 328/328
 317/480
 692/844
 1439/2204
 1338/29361
 450/450
 N_e
 events / total
 112/559
 97/1888
 Follow up
 1990-2004
 1991-2002
 1993-1996
 1983-1996
 2001- 2002
 1989-1992
 1996-1997
 2000-2003
 1982-1988
 1993-2001
 1993-1998
 Follow up
 2000-2007
 1943-1966
 Country
 Australia
 Italy
 The USA
 The USA
 China
 UK
 New Zealand
 The USA
 The USA
 The USA
 The USA
 Country
 The USA
 Australia
 Author, year [ref]
 Beilby
 et al.
 2010 [
 29

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 Bosetti
 et al.
 2004 [32
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 Gill
 et al.
 2009 [22
]
 Goodman
 et al.
 2003 [23
]
 Jian
 et al.
 2004 [34
]
 Key
 et al.
 1997 [33
]
 Norrish
 et al.
 2000 [31
]
 Peters
 et al.
 2007 [24
]
 Cook
 et al.
 1999 [25
]
 Kirsh
 et al.
 2006 [27
]
 Wu
 et al.
 2004 [26
]
 Author, year [ref]
 Nordström
 et al.
 2016 [28
]
 Ambrosini
 et al.
 2007 [30
]

Table
2

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Summary of results

Analysis
 No
 of studies (datasets) [ref]
 Model
 OR [95% CI]
 Z-test
 Heterogeneity
 Publication bias
 (
 P
 value)
 I
 2
 (%)
 Tau
 2

Chi

2

Begg's test

Egger's test

Lycopene

11 (15) [

ADDIN ZOTERO_ITEM CSL_CITATION {"citationID":"GHUFus0v","properties":{"formattedCitation":"\u002222-24,26-29,31-34\u0022","plainCitation":"22-24,26-29,31-34","noteIndex":0},"citationItems":[{"id":764,"uris":["http://zotero.org/users/2724931/items/KKJLTJHE"],"uri":["http://zotero.org/users/2724931/items/KKJLTJHE"],"itemData":{"id":764,"type":"article-journal","title":"Association of selenium, tocopherols, carotenoids, retinol, and 15-isoprostane F(2t) in serum or urine with prostate cancer risk: the multiethnic cohort","container-title":"Cancer causes & control : CCC","page":"1161-1171","volume":"20","issue":"7","archive":"PMC","archive_location":"PMC2725220","abstract":"OBJECTIVE: We examine the association of antioxidants and 15-isoprostane F(2t) with risk of prostate cancer. METHODS: We conducted a nested case-control study of serum antioxidant biomarkers (selenium, tocopherols, carotenoids, and retinol) and a urinary oxidation biomarker (15-isoprostane F(2t)) with risk of prostate cancer within the Multiethnic Cohort. Demographic, dietary, and other exposure information was collected by self-administered questionnaire in 1993-1996. We compared prediagnostic biomarker levels from 467 prostate cancer cases and 936 cancer free controls that were matched on several variables. Multivariate conditional logistic regression models were used to compute adjusted odds ratios (ORs) and 95% confidence intervals (CIs). RESULTS: We observed that there was no overall association of serum concentrations of antioxidants and urinary concentrations of 15-isoprostane F(2t) with risk of prostate cancer or risk of advanced prostate cancer. However, we did observe an inverse association for serum selenium only among African-American men (p trend = 0.02); men in the third tertile of selenium concentrations had a 41% lower risk (95% CI: 0.38-0.93) of prostate cancer when compared to men in the first tertile. CONCLUSIONS: Overall, our study found no association of serum antioxidants or 15-isoprostane F(2t) with the risk of prostate cancer. The observed inverse association of selenium with prostate cancer in African-Americans needs to be validated in other studies."},"DOI":"10.1007/s10552-009-9304-4","ISSN":"0957-5243","author":{"family":"Gill","given":"Jasmeet K"}, {"family":"Franke","given":"Adrian A"}, {"family":"Morris","given":"J Steven"}, {"family":"Cooney","given":"Robert V"}, {"family":"Wilkens","given":"Lynne R"}, {"family":"Le Marchand","given":"Loic"}, {"family":"Goodman","given":"Marc T"}, {"family":"Henderson","given":"Brian E"}, {"family":"Kolonel","given":"Laurence N"}],"issued":{"date-parts":["2009,9"]}}, {"id":767,"uris":["http://zotero.org/users/2724931/items/G2VXZNAR"],"uri":["http://zotero.org/users/2724931/items/G2VXZNAR"],"itemData":{"id":767,"type":"article-journal","title":"The Association between Lung and Prostate Cancer Risk, and Serum Micronutrients","container-title":"Cancer Epidemiology Biomarkers & Prevention","page":"518","volume":"12","issue":"6","abstract":"\u0022Carotene and Retinol Efficacy Trial is a nationwide chemoprevention trial that recruited 18,314 high-risk individuals to test the effect of supplemental \u0022carotene and retinol on lung cancer incidence. In this report, we conducted a prospective nested case-control study of the association between serum carotenoids, retinoids, and tocopherols on both lung and prostate cancer incidence. Prerandomization serum samples were selected from 278 lung cancer cases and 205 prostate cancer cases, and 483 controls matched by high-risk population, study center location, age, sex (lung cancer only), smoking status, and year of randomization. Carotenoids, retinoids, and tocopherols were analyzed by high-performance liquid chromatography. Endpoints were confirmed by pathology review (lung cancer) or review of the pathology report (prostate cancer). In the control-only population, there was a significant association between tobacco use and serum micronutrient concentration. Current smokers compared with former smokers had lower mean levels of all of the micronutrients tested with zeaxanthin, \u0022cryptoxanthin, \u0022carotene, \u0022tocopherol, retinol, and retinyl palmitate reaching statistical significance at P = 0.05. In the overall population, the mean serum concentrations of all of the micronutrients except \u0022tocopherol were lower for lung cancer cases than controls. Statistically significant trends across quartiles were observed in lutein (P = 0.02), zeaxanthin (P = 0.02), and \u0022tocopherol (P = 0.03). The carotenoid findings in the overall population were because of the strong inverse association between serum micronutrients and lung cancer in females. Statistically significant odds ratios (ORs) comparing 4th to 1st quartiles in the female population were seen in lutein [OR, 0.31; confidence interval (CI), 0.13-0.75], zeaxanthin (OR, 0.31; CI, 0.12-0.77), and \u0022cryptoxanthin (OR, 0.34; CI, 0.14-0.81). For prostate cancer, mean serum concentrations were lower in cases for all of the nutrients except \u0022carotene. Only for \u0022tocopherol (Ptrend = 0.04) were the findings statistically significant. There was no statistically significant association between serum carotenoids and prostate cancer. Our findings provide additional support for the association between physiological levels of dietary micronutrients and cancer incidence."},"journalAbbreviation":"Cancer Epidemiol Biomarkers Prev","author":{"family":"Goodman","given":"Gary E."}, {"family":"Schaffer","given":"Steven"}, {"family":"Omenn","given":"Gilbert S."}, {"family":"Chen","given":"Chu"}, {"family":"King","given":"Irena"}],"issued":{"date-parts":["2003,6,1"]}}, {"id":775,"uris":["http://zotero.org/users/2724931/items/6GDCVHDT"],"uri":["http://zotero.org/users/2724931/items/6GDCVHDT"],"itemData":{"id":775,"type":"article-journal","title":"Serum Lycopene, Other Carotenoids, and Prostate Cancer Risk: a Nested Case-Control Study in

the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial", "container-title": "Cancer Epidemiology Biomarkers & Prevention", "page": "962", "volume": "16", "issue": "5", "abstract": "Background: Reports from several studies have suggested that carotenoids, and in particular lycopene, could be prostate cancer-preventive agents. This has stimulated extensive laboratory and clinical research, as well as much commercial and public enthusiasm. However, the epidemiologic evidence remains inconclusive. Materials and Methods: We investigated the association between prediagnostic serum carotenoids (lycopene,

α

-carotene,

β

-carotene,

β

-cryptoxanthin, lutein, and zeaxanthin) and risk of prostate cancer in the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial, a multicenter study designed to examine methods of early detection and risk factors for cancer. The study included 692 incident prostate cancer cases, diagnosed 1 to 8 years after study entry, including 270 aggressive cases, with regional or distant stage ($n = 90$) or Gleason score ≥ 7 ($n = 235$), and 844 randomly selected, matched controls. As study participants were selected from those who were assigned to annual standardized screening for prostate cancer, results are unlikely to be biased by differential screening, a circumstance that is difficult to attain under non-trial conditions. Results: No association was observed between serum lycopene and total prostate cancer [odds ratios (OR), 1.14; 95% confidence intervals (95% CI), 0.82-1.58 for highest versus lowest quintile; P for trend, 0.28] or aggressive prostate cancer (OR, 0.99; 95% CI, 0.62-1.57 for highest versus lowest quintile; P for trend, 0.433).

β

-Carotene was associated with an increased risk of aggressive prostate cancer (OR, 1.67; 95% CI, 1.03-2.72 for highest versus lowest quintile; P for trend, 0.13); in particular, regional or distant stage disease (OR, 3.16; 95% CI, 1.37-7.31 for highest versus lowest quintile; P for trend, 0.02); other carotenoids were not associated with risk. Conclusion: In this large prospective study, high serum

β

-carotene concentrations were associated with increased risk for aggressive, clinically relevant prostate cancer. Lycopene and other carotenoids were unrelated to prostate cancer. Consistent with other recent publications, these results suggest that lycopene or tomato-based regimens will not be effective for prostate cancer prevention.

(Cancer Epidemiol Biomarkers Prev 2007;16(5):962-8)", "DOI": "10.1158/1055-9965.EPI-06-

0861", "journalAbbreviation": "Cancer Epidemiol Biomarkers Prev", "author":

{{"family": "Peters", "given": "Ulrike"}, {"family": "Leitzmann", "given": "Michael F."},

{{"family": "Chatterjee", "given": "Nilanjan"}, {"family": "Wang", "given": "Yinghui"},

{{"family": "Albanes", "given": "Demetrius"}, {"family": "Germann", "given": "Edward P."},

{{"family": "Friesen", "given": "Marlin D."}, {"family": "Riboli", "given": "Elio"}, {"family": "Hayes", "given": "Richard B."}}, "issued": {"date-parts": [{"2007", "5", "1"}]}, {"id": "776", "uris":

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Epidemiology Biomarkers & Prevention", "page": "260", "volume": "13", "issue": "2", "abstract": "The

association between plasma carotenoids and prostate cancer risk was investigated in a case-control study nested within the prospective Health Professionals Follow-up Study. We matched 450 incident prostate cancer cases diagnosed from 1993-1998 to 450 controls by age, time, month, and year of blood donation. Modest inverse, but not statistically significant, associations were observed among plasma

α

-carotene,

β

-carotene, and lycopene concentrations, and overall risk of prostate cancer diagnosis {odds ratio (highest versus lowest quintile; OR),

α

-carotene: OR, 0.67 [95% confidence interval (CI), -0.40-1.09];

β

-carotene: OR, 0.78 (95% CI, 0.48-1.25); lycopene: OR, 0.66 (95% CI, 0.38-1.13)}. The inverse association between plasma lycopene concentrations and prostate cancer risk was limited to participants who were 65 years or older (OR, 0.47; 95% CI, 0.23-0.98) and without a family history of prostate cancer (OR, 0.48; 95% CI, 0.26-0.89). Combining, older age and a negative family history provided similar results (OR, 0.43; 95% CI, 0.18-1.02). Inverse associations between

β

-carotene and prostate cancer risk were also found among younger participants (<65 years of age; OR, 0.36; 95% CI, 0.14-0.91; P trend = 0.03). Combining dietary intake and plasma data confirmed our results. We found a statistically significant inverse association between higher plasma lycopene concentrations and lower risk of prostate cancer, which was restricted to older participants and those without a family history of prostate cancer. This observation suggests that tomato products may exhibit more potent protection against sporadic prostate cancer rather than those with a stronger familial or hereditary component. In addition, our findings also suggest that among younger men, diets rich in

β

-carotene may also play a protective role in prostate carcinogenesis.", "DOI": "10.1158/1055-9965.EPI-03-

0012", "journalAbbreviation": "Cancer Epidemiol Biomarkers Prev", "author": [{"family": "Wu", "given": "Kana"},

{{"family": "Erdman", "given": "John W."}, {"family": "Schwartz", "given": "Steven J."},

{{"family": "Platz", "given": "Elizabeth A."}, {"family": "Leitzmann", "given": "Michael"},

{{"family": "Clinton", "given": "Steven K."}, {"family": "DeGroot", "given": "Valerie"},

{{"family": "Willett", "given": "Walter C."}, {"family": "Giovannucci", "given": "Edward"}], "issued": {"date-parts":

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Prospective Study of Lycopene and Tomato Product Intake and Risk of Prostate Cancer", "container-title": "Cancer

Epidemiology Biomarkers & Prevention", "page": "92", "volume": "15", "issue": "1", "abstract": "Background:

Dietary lycopene and tomato products may reduce risk of prostate cancer; however, uncertainty remains about this possible association. Methods: We evaluated the association between intake of lycopene and specific tomato products and prostate cancer risk in the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial, a multicenter study designed to investigate cancer early detection methods and etiologic determinants. Participants completed both a general risk factor and a 137-item food frequency questionnaire at baseline. A total of 1,338

cases of prostate cancer were identified among 29,361 men during an average of 4.2 years of follow-up. Results: Lycopene intake was not associated with prostate cancer risk. Reduced risks were also not found for total tomato servings or for most tomato-based foods. Statistically nonsignificant inverse associations were noted for pizza [all prostate cancer: relative risk (RR), 0.83; 95% confidence interval (95% CI), 0.67-1.03 for ≥ 1 serving/wk versus < 0.5 serving/mo; P_{trend} = 0.06 and advanced prostate cancer: RR, 0.79; 95% CI, 0.56-1.10; P_{trend} = 0.12] and spaghetti/tomato sauce consumption (advanced prostate cancer: RR = 0.81, 95% CI, 0.57-1.16 for ≥ 2 servings/wk versus < 1 serving/mo; P_{trend} = 0.31). Among men with a family history of prostate cancer, risks were decreased in relation to increased consumption of lycopene (P_{trend} = 0.04) and specific tomato-based foods commonly eaten with fat (spaghetti, P_{trend} = 0.12; pizza, P_{trend} = 0.15; lasagna, P_{trend} = 0.02). Conclusions: This large study does not support the hypothesis that greater lycopene/tomato product consumption protects from prostate cancer. Evidence for protective associations in subjects with a family history of prostate cancer requires further corroboration. (Cancer Epidemiol Biomarkers Prev 2006;15(1):92-8), "DOI": "10.1158/1055-9965.EPI-05-0563", "journalAbbreviation": "Cancer Epidemiol Biomarkers Prev", "author": [{"family": "Kirsh", "given": "Victoria A."}, {"family": "Mayne", "given": "Susan T."}, {"family": "Peters", "given": "Ulrike"}, {"family": "Chatterjee", "given": "Nilanjan"}, {"family": "Leitzmann", "given": "Michael F."}, {"family": "Dixon", "given": "L. Beth"}, {"family": "Urban", "given": "Donald A."}, {"family": "Crawford", "given": "E. David"}, {"family": "Hayes", "given": "Richard B."}], "issued": {"date-parts": [{"2006", 1, 1}]}, {"id": "772", "uris": ["http://zotero.org/users/2724931/items/Z88XYJCK"], "uri": ["http://zotero.org/users/2724931/items/Z88XYJCK"], "itemData": {"id": "772", "type": "article-journal", "title": "Associations Between Circulating Carotenoids, Genomic Instability and the Risk of High-Grade Prostate Cancer", "container-title": "The Prostate", "page": "339-348", "volume": "76", "issue": "4", "archive": "PMC", "archive_location": "PMC5493324", "abstract": "BACKGROUND: Carotenoids are a class of nutrients with antioxidant properties that have been purported to protect against cancer. However, the reported associations between carotenoids and prostate cancer have been heterogeneous and lacking data on interactions with nucleotide sequence variations and genomic biomarkers. OBJECTIVE: To examine the associations between carotenoid levels and the risk of high-grade prostate cancer, also considering antioxidant-related genes and tumor instability. METHODS: We measured plasma levels of carotenoids and genotyped 20 single nucleotide polymorphisms (SNP) in SOD1, SOD2, SOD3, XRCC1, and OGG1 among 559 men with non-metastatic prostate cancer undergoing radical prostatectomy. We performed copy number analysis in a subset of these men (n = 67) to study tumor instability assessed as Fraction of the Genome Altered (FGA). We examined associations between carotenoids, genotypes, tumor instability and risk of high-grade prostate cancer (Gleason grade $\geq 4 + 3$) using logistic and linear regression. RESULTS: Circulating carotenoid levels were inversely associated with the risk of high-grade prostate cancer; odds ratios (OR) and 95% confidence intervals (CI) comparing highest versus lowest quartiles were: 0.34 (95% CI: 0.18-0.66) for α -carotene, 0.31 (95% CI: 0.15-0.63) for β -carotene, 0.55 (0.28-1.08) for lycopene and 0.37 (0.18-0.75) for total carotenoids. SNPs rs25489 in XRCC1, rs699473 in SOD3 and rs1052133 in OGG1 modified these associations for α -carotene, β -carotene and lycopene, respectively (P ≤ 0.05). The proportion of men with a high degree of FGA increased with Gleason Score (P < 0.001). Among men with Gleason score $\leq 3 + 4$, higher lycopene levels were associated with lower FGA (P = 0.04). CONCLUSION: Circulating carotenoids at diagnosis, particularly among men carrying specific somatic variations, were inversely associated with risk of high-grade prostate cancer. In exploratory analyses, higher lycopene level was associated with less genomic instability among men with low-grade disease which is novel and supports the hypothesis that lycopene may inhibit progression of prostate cancer early in its natural history.", "DOI": "10.1002/pros.23125", "ISSN": "0270-4137", "author": [{"family": "Nordström", "given": "Tobias"}, {"family": "Van Blarigan", "given": "Erin L"}, {"family": "Ngo", "given": "Vy"}, {"family": "Roy", "given": "Ritu"}, {"family": "Weinberg", "given": "Vivian"}, {"family": "Song", "given": "Xiaoling"}, {"family": "Simko", "given": "Jeffrey"}, {"family": "Carroll", "given": "Peter R"}, {"family": "Chan", "given": "June M"}, {"family": "Paris", "given": "Pamela L"}], "issued": {"date-parts": [{"2016", 3, 1}]}, {"id": "759", "uris": ["http://zotero.org/users/2724931/items/UC8EM9WV"], "uri": ["http://zotero.org/users/2724931/items/UC8EM9WV"], "itemData": {"id": "759", "type": "article-journal", "title": "Serum levels of folate, lycopene, β -carotene, retinol and vitamin E and prostate cancer risk", "container-title": "European Journal Of Clinical Nutrition", "page": "1235", "volume": "64", "journalAbbreviation": "European Journal Of Clinical Nutrition", "author": [{"family": "Beilby", "given": "J"}, {"family": "Ambrosini", "given": "G L"}, {"family": "Rossi", "given": "E"}, {"family": "Klerk", "given": "N H", "non-dropping-particle": "de"}, {"family": "Musk", "given": "A W"}], "issued": {"date-parts": [{"2010", 8, 4}]}, {"id": "773", "uris": ["http://zotero.org/users/2724931/items/M8ZPITDZ"], "uri": ["http://zotero.org/users/2724931/items/M8ZPITDZ"], "itemData": {"id": "773", "type": "article-journal", "title": "Prostate Cancer and Dietary Carotenoids", "container-title": "American Journal of Epidemiology", "page": "119-123", "volume": "151", "issue": "2", "abstract": "This population-based case-control study investigated associations between prostate cancer risk and dietary intake of the carotenoids β -carotene and lycopene and their major plant food sources, including carrots, green leafy vegetables, and tomato-based foods. The study was carried out in Auckland, New Zealand, during 1996-1997 and recruited 317 prostate cancer cases and 480 controls. The authors found that dietary intake of β -carotene and its main vegetable sources was largely unassociated with prostate cancer risk, whereas intake of lycopene and tomato-based foods was weakly associated with a reduced risk. These results suggest that in contrast to the findings regarding many types of cancers, vegetables rich in β -carotene are not protective against prostate cancer. However, lycopene from tomato-based foods was found to be associated with a small reduction in risk. Am J Epidemiol 2000; 151:119-23.", "DOI": "10.1093/oxfordjournals.aje.a010176", "ISSN": "0002-9262", "journalAbbreviation": "American Journal of Epidemiology", "author": [{"family": "Norris", "given": "Alan E."}, {"family": "Jackson", "given": "Rodney T."}, {"family": "Sharpe", "given": "Susan J."}, {"family": "Skeaff", "given": "C. Murray"}], "issued": {"date-parts":

[["2000",1,15]]}],{"id":760,"uris":["http://zotero.org/users/2724931/items/2YX9MMBA"],"uri":["http://zotero.org/users/2724931/items/2YX9MMBA"],"itemData":{"id":760,"type":"article-journal","title":"Retinol, carotenoids and the risk of prostate cancer: A case-control study from Italy","container-title":"International Journal of Cancer","page":"689-692","volume":"112","issue":"4","abstract":"Abstract Several studies have evaluated the possible association between intakes of retinoids and carotenoids and the risk of prostate cancer, but the evidence is still inconsistent. Further, only a few studies have investigated the role of specific carotenoids other than β -carotene. We have thus considered the association between retinol and various carotenoids using data from a multicentric case-control study conducted in Italy between 1991 and 2002. This included 1,294 incident, histologically confirmed prostate cancer cases below age 75 years admitted to major teaching and general hospitals in the areas under study, and 1,451 controls below age 75 years selected among patients admitted to the same hospitals as cases for a wide spectrum of acute nonneoplastic conditions not related to long-term modifications of diet. Subjects' usual diet was investigated by means of a validated food-frequency questionnaire. Multivariate odds ratios and the corresponding 95% confidence intervals were estimated using unconditional logistic regression models. The risk of prostate cancer tended to decrease with increasing intake of retinol (OR = 0.79 for the highest versus the lowest quintile of intake), carotene (OR = 0.70), α -carotene (OR = 0.85) and β -carotene (OR = 0.72), although the estimates were significant for carotene and β -carotene only. No meaningful associations emerged for nonprovitamin A carotenoids, such as lycopene (OR = 0.94) and lutein/zeaxanthin (OR = 0.91). No systematic heterogeneity was observed across strata of age, education and body mass index. Thus, our study supports the hypothesis of a weak protective effect of carotene, particularly β -carotene, on the risk of prostate cancer, while it indicates that other carotenoids, including lycopene, and retinol are not appreciably related to the risk of this neoplasm. ? 2004 Wiley-Liss, Inc.", "DOI": "10.1002/ijc.20486", "ISSN": "0020-7136", "journalAbbreviation": "International Journal of Cancer", "author": [{"family": "Bosetti", "given": "Cristina"}, {"family": "Talamini", "given": "Renato"}, {"family": "Montella", "given": "Maurizio"}, {"family": "Negri", "given": "Eva"}, {"family": "Conti", "given": "Ettore"}, {"family": "Franceschi", "given": "Silvia"}, {"family": "La Vecchia", "given": "Carlo"}], "issued": {"date-parts": [{"2004", 7, 9}]}}, {"id":770,"uris":["http://zotero.org/users/2724931/items/VCIH4USS"],"uri":["http://zotero.org/users/2724931/items/VCIH4USS"],"itemData":{"id":770,"type":"article-journal","title":"A case-control study of diet and prostate cancer.", "container-title": "British Journal of Cancer", "page": "678-687", "volume": "76", "issue": "5", "archive": "PMC", "archive_location": "PMC2228001", "abstract": "We interviewed 328 men diagnosed with prostate cancer before the age of 75 years and 328 age-matched population controls. The principal hypotheses were that risk would increase with a high intake of total or saturated fat and would decrease with a high intake of carotene (beta-carotene equivalents) or lycopene. We also examined the associations of other nutrients and foods with risk. There was no evidence for an association between fat intake and risk, although the average fat intake was high and the range of fat intakes was narrow (medians of lower and upper thirds of percentage of energy from fat among controls were 34.3% and 42.9% respectively). Risk was lower in subjects with higher carotene intake: odds ratios 0.65 (95% CI 0.45-0.94) and 0.76 (0.53-1.10) in the middle and upper thirds of carotene intake respectively (P for trend = 0.150). Lycopene was not associated with risk. Among 13 other nutrients examined, the odds ratios in the top third of intake were below 0.8 for: potassium, 0.74 (0.51-1.09; P for trend = 0.054); zinc, 0.73 (0.49-1.08; P for trend = 0.126); iodine, 0.75 (0.51-1.11; P for trend = 0.077); vitamin B6 food only, 0.77 (0.53-1.12; P for trend = 0.077); and vitamin B6 including supplements, 0.70 (0.48-1.03; P for trend = 0.029). Among 18 foods examined, statistically significant associations were observed for: garlic as food, > or = 2/week vs never, 0.56 (0.33-0.93); garlic including supplements, > or = 2/week vs never, 0.60 (0.37-0.96); baked beans, > or = 2/week vs < 1/month, 0.57 (0.34-0.95); and garden peas, > or = 5/week vs < or = 3/month, 0.35 (0.13-0.91). This study does not support the hypothesis that fat increases risk and is equivocal in relation to carotene. The possible relationships of vitamin B6, garlic, beans and peas with risk for prostate cancer should be further investigated.", "ISSN": "0007-0920", "author": [{"family": "Key", "given": "T J"}, {"family": "Silcocks", "given": "P B"}, {"family": "Davey", "given": "G K"}, {"family": "Appleby", "given": "P N"}, {"family": "Bishop", "given": "D T"}], "issued": {"date-parts": [{"1997"}]}}, {"id":768,"uris":["http://zotero.org/users/2724931/items/84P4HPA6"],"uri":["http://zotero.org/users/2724931/items/84P4HPA6"],"itemData":{"id":768,"type":"article-journal","title":"Do dietary lycopene and other carotenoids protect against prostate cancer?", "container-title": "International Journal of Cancer", "page": "1010-1014", "volume": "113", "issue": "6", "abstract": "Abstract To determine whether dietary intake of lycopene and other carotenoids has an etiological association with prostate cancer, a case?control study was conducted in Hangzhou, southeast China during 2001?2002. The cases were 130 incident patients with histologically confirmed adenocarcinoma of the prostate. The controls were 274 hospital inpatients without prostate cancer or any other malignant diseases. Information on usual food consumption, including vegetables and fruits, was collected by face-to-face interviews using a structured food frequency questionnaire. The risks of prostate cancer for the intake of carotenoids and selected vegetables and fruits rich in carotenoids were assessed using multivariate logistic regression, adjusting for age, locality, education, income, body mass index, marital status, number of children, family history of prostate cancer, tea drinking, total fat and caloric intake. The prostate cancer risk declined with increasing consumption of lycopene, α -carotene, β -carotene, β -cryptoxanthin, lutein and zeaxanthin. Intake of tomatoes, pumpkin, spinach, watermelon and citrus fruits were also inversely associated with the prostate cancer risk. The adjusted odds ratios for the highest versus the lowest quartiles of intake were 0.18 (95% CI: 0.08?0.41) for lycopene, 0.43 (95% CI: 0.21?0.85) for α -carotene, 0.34 (95% CI: 0.17?0.69) for β -carotene, 0.15 (95% CI: 0.06?0.34) for β -cryptoxanthin and 0.02 (95% CI: 0.01?0.10) for lutein and zeaxanthin. The corresponding dose?response relationships were also significant, suggesting that vegetables and fruits rich in lycopene and other carotenoids may be protective against prostate cancer. ? 2004 Wiley-Liss, Inc.", "DOI": "10.1002/ijc.20667", "ISSN": "0020-7136", "journalAbbreviation": "International Journal of Cancer", "author": [{"family": "Jian", "given": "Le"}, {"family": "Du", "given": "Chuan-Jun"}, {"family": "Lee", "given": "Andy H."}, {"family": "Binns", "given": "Colin W."}], "issued": {"date-parts": [{"2004", 10, 28}]}}, {"schema": "https://github.com/citation-style-language/schema/raw/master/csl-citation.json"}]

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 CCC","page":"1161-
 1171","volume":"20","issue":"7","archive":"PMC","archive_location":"PMC2725220","abstract":"OBJECTIVE:
 We examine the association of antioxidants and 15-isoprostane F(2t) with risk of prostate cancer. METHODS: We
 conducted a nested case–control study of serum antioxidant biomarkers (selenium, tocopherols, carotenoids, and
 retinol) and a urinary oxidation biomarker (15-isoprostane F(2t)) with risk of prostate cancer within the
 Multiethnic Cohort. Demographic, dietary, and other exposure information was collected by self-administered
 questionnaire in 1993–1996. We compared prediagnostic biomarker levels from 467 prostate cancer cases and 936
 cancer free controls that were matched on several variables. Multivariate conditional logistic regression models
 were used to compute adjusted odds ratios (ORs) and 95% confidence intervals (CIs). RESULTS: We observed
 that there was no overall association of serum concentrations of antioxidants and urinary concentrations of 15-
 isoprostane F(2t) with risk of prostate cancer or risk of advanced prostate cancer. However, we did observe an
 inverse association for serum selenium only among African-American men (p trend = 0.02); men in the third
 tertile of selenium concentrations had a 41% lower risk (95% CI: 0.38–0.93) of prostate cancer when compared to
 men in the first tertile. CONCLUSIONS: Overall, our study found no association of serum antioxidants or 15-
 isoprostane F(2t) with the risk of prostate cancer. The observed inverse association of selenium with prostate
 cancer in African-Americans needs to be validated in other studies.","DOI":"10.1007/s10552-009-
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 Association between Lung and Prostate Cancer Risk, and Serum Micronutrients","container-title":"Cancer
 Epidemiology Biomarkers & Prevention","page":"518","volume":"12","issue":"6","abstract":"
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 -Carotene and Retinol Efficacy Trial is a nationwide chemoprevention trial that recruited 18,314 high-risk
 individuals to test the effect of supplemental
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 -carotene and retinol on lung cancer incidence. In this report, we conducted a prospective nested case-control
 study of the association between serum carotenoids, retinoids, and tocopherols on both lung and prostate cancer
 incidence. Prerandomization serum samples were selected from 278 lung cancer cases and 205 prostate cancer
 cases, and 483 controls matched by high-risk population, study center location, age, sex (lung cancer only),
 smoking status, and year of randomization. Carotenoids, retinoids, and tocopherols were analyzed by high-
 performance liquid chromatography. Endpoints were confirmed by pathology review (lung cancer) or review of
 the pathology report (prostate cancer). In the control-only population, there was a significant association between
 tobacco use and serum micronutrient concentration. Current smokers compared with former smokers had lower
 mean levels of all of the micronutrients tested with zeaxanthin,
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 -cryptoxanthin,
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 -carotene,
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 -tocopherol, retinol, and retinyl palmitate reaching statistical significance at P = 0.05. In the overall population, the
 mean serum concentrations of all of the micronutrients except
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 -tocopherol were lower for lung cancer cases than controls. Statistically significant trends across quartiles were
 observed in lutein (P = 0.02), zeaxanthin (P = 0.02), and
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 -tocopherol (P = 0.03). The carotenoid findings in the overall population were because of the strong inverse
 association between serum micronutrients and lung cancer in females. Statistically significant odds ratios (ORs)
 comparing 4th to 1st quartiles in the female population were seen in lutein [OR, 0.31; confidence interval (CI),
 0.13–0.75], zeaxanthin (OR, 0.31; CI, 0.12–0.77), and
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-cryptoxanthin (OR, 0.34; CI, 0.14–0.81). For prostate cancer, mean serum concentrations were lower in cases for all of the nutrients except

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-carotene. Only for

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-tocopherol (Ptrend = 0.04) were the findings statistically significant. There was no statistically significant association between serum carotenoids and prostate cancer. Our findings provide additional support for the association between physiological levels of dietary micronutrients and cancer incidence.", "journalAbbreviation": "Cancer Epidemiol Biomarkers Prev", "author":

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-cryptoxanthin, lutein, and zeaxanthin) and risk of prostate cancer in the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial, a multicenter study designed to examine methods of early detection and risk factors for cancer. The study included 692 incident prostate cancer cases, diagnosed 1 to 8 years after study entry, including 270 aggressive cases, with regional or distant stage (n = 90) or Gleason score ≥ 7 (n = 235), and 844 randomly selected, matched controls. As study participants were selected from those who were assigned to annual standardized screening for prostate cancer, results are unlikely to be biased by differential screening, a circumstance that is difficult to attain under non-trial conditions. Results: No association was observed between serum lycopene and total prostate cancer [odds ratios (OR), 1.14; 95% confidence intervals (95% CI), 0.82–1.58 for highest versus lowest quintile; P for trend, 0.28] or aggressive prostate cancer (OR, 0.99; 95% CI, 0.62–1.57 for highest versus lowest quintile; P for trend, 0.433).

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-Carotene was associated with an increased risk of aggressive prostate cancer (OR, 1.67; 95% CI, 1.03–2.72 for highest versus lowest quintile; P for trend, 0.13); in particular, regional or distant stage disease (OR, 3.16; 95% CI, 1.37–7.31 for highest versus lowest quintile; P for trend, 0.02); other carotenoids were not associated with risk. Conclusion: In this large prospective study, high serum

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-carotene concentrations were associated with increased risk for aggressive, clinically relevant prostate cancer. Lycopene and other carotenoids were unrelated to prostate cancer. Consistent with other recent publications, these results suggest that lycopene or tomato-based regimens will not be effective for prostate cancer prevention.

(Cancer Epidemiol Biomarkers Prev 2007;16(5):962–8)", "DOI": "10.1158/1055-9965.EPI-06-0861", "journalAbbreviation": "Cancer Epidemiol Biomarkers Prev", "author": [{"family": "Peters", "given": "Ulrike"}, {"family": "Leitzmann", "given": "Michael F."}, {"family": "Chatterjee", "given": "Nilanjan"}, {"family": "Wang", "given": "Yinghui"}, {"family": "Albanes", "given": "Demetrius"}, {"family": "Germann", "given": "Edward P."}, {"family": "Friesen", "given": "Marlin D."}, {"family": "Riboli", "given": "Elio"}, {"family": "Hayes", "given": "Richard B."}], "issued": {"date-parts": [{"2007", 5, 1}]}, {"id": "762", "uris":

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-carotene supplementation for patients with low baseline levels and decreased risks of total and prostate carcinoma", "container-title": "Cancer", "page": "1783–1792", "volume": "86", "issue": "9", "abstract": "Abstract BACKGROUND The Physicians' Health Study was a randomized, double-blind, placebo-controlled trial using a 2 ? 2 factorial design including supplementation with ?-carotene (50 mg every other day) in the primary prevention of cancer among 22,071 U.S. male physicians ages 40?84 years at randomization. Before randomization, the authors collected baseline blood specimens to determine whether any benefit was greater among or confined to those with low baseline levels of ?-carotene. METHODS Baseline blood samples were collected from 14,916 participants. These samples were assayed, according to a nested case?control design, from 1439 men subsequently diagnosed with cancer over 12 years of follow-up (631 with prostate carcinoma) and 2204 controls matched by age and smoking habits. RESULTS Men in the lowest quartile for plasma ?-carotene at baseline had a marginally significant (P = 0.07) increased risk of cancer compared with those in the highest quartile (relative risk [RR] = 1.30, 95% confidence interval [CI], 0.98?1.74). Men in the lowest quartile assigned at random to ?-carotene supplementation had a possible but nonsignificant decrease in overall cancer risk (RR = 0.83, 95% CI, 0.63?1.09) compared with those assigned to placebo. This was primarily due to a significant reduction in the risk of prostate carcinoma (RR = 0.68, 95% CI, 0.46?0.99) in this group. After the first 2 years of follow-up were excluded, the results were virtually unchanged. CONCLUSIONS These prespecified subgroup analyses appeared to support the idea that ?-carotene supplementation may reduce risk of prostate carcinoma among those with low baseline levels. Further follow-up of this population will help determine whether these findings are valid. [See editorial on pages 1629?31, this issue.] Cancer 1999;86:1783?92. ? 1999 American Cancer Society.", "DOI": "10.1002/(SICI)1097-0142(19991101)86:9<1783::AID-CNCR21>3.0.CO;2-N", "ISSN": "0008-543X", "journalAbbreviation": "Cancer", "author": [{"family": "Cook", "given": "Nancy R."}, {"family": "Stampfer", "given": "Meir J."}, {"family": "Ma", "given": "Jing"}, {"family": "Manson", "given": "JoAnn E."}, {"family": "Sacks", "given": "Frank M."}, {"family": "Buring", "given": "Julie E."}, {"family": "Hennekens", "given": "Charles H."}], "issued": {"date-parts": [{"2000", 11, 20}]}, {"id": "776", "uris":

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Epidemiology Biomarkers & Prevention", "page": "260", "volume": "13", "issue": "2", "abstract": "The association between plasma carotenoids and prostate cancer risk was investigated in a case-control study nested within the prospective Health Professionals Follow-up Study. We matched 450 incident prostate cancer cases diagnosed from 1993–1998 to 450 controls by age, time, month, and year of blood donation. Modest inverse, but not statistically significant, associations were observed among plasma

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-carotene, and lycopene concentrations, and overall risk of prostate cancer diagnosis {odds ratio (highest versus lowest quintile; OR),

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-carotene: OR, 0.67 [95% confidence interval (CI), -0.40–1.09];

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-carotene: OR, 0.78 (95% CI, 0.48–1.25); lycopene: OR, 0.66 (95% CI, 0.38–1.13)}. The inverse association between plasma lycopene concentrations and prostate cancer risk was limited to participants who were 65 years or older (OR, 0.47; 95% CI, 0.23–0.98) and without a family history of prostate cancer (OR, 0.48; 95% CI, 0.26–0.89). Combining, older age and a negative family history provided similar results (OR, 0.43; 95% CI, 0.18–1.02). Inverse associations between

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-carotene and prostate cancer risk were also found among younger participants (<65 years of age; OR, 0.36; 95% CI, 0.14–0.91; P -trend = 0.03). Combining dietary intake and plasma data confirmed our results. We found a statistically significant inverse association between higher plasma lycopene concentrations and lower risk of prostate cancer, which was restricted to older participants and those without a family history of prostate cancer. This observation suggests that tomato products may exhibit more potent protection against sporadic prostate cancer rather than those with a stronger familial or hereditary component. In addition, our findings also suggest that among younger men, diets rich in

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-carotene may also play a protective role in prostate carcinogenesis.", "DOI": "10.1158/1055-9965.EPI-03-0012", "journalAbbreviation": "Cancer Epidemiol Biomarkers Prev", "author": [{"family": "Wu", "given": "Kana"}, {"family": "Erdman", "given": "John W."}, {"family": "Schwartz", "given": "Steven J."}, {"family": "Platz", "given": "Elizabeth A."}, {"family": "Leitzmann", "given": "Michael"}, {"family": "Clinton", "given": "Steven K."}, {"family": "DeGroot", "given": "Valerie"}, {"family": "Willett", "given": "Walter C."}, {"family": "Giovannucci", "given": "Edward"}], "issued": {"date-parts": [{"2004", 2, 1}]}, {"id": "772", "uris": [{"http://zotero.org/users/2724931/items/Z88XYJCK"}], "uri": [{"http://zotero.org/users/2724931/items/Z88XYJCK"}], "itemData": {"id": "772", "type": "article-journal", "title": "Associations Between Circulating Carotenoids, Genomic Instability and the Risk of High-Grade Prostate Cancer", "container-title": "The Prostate", "page": "339-348", "volume": "76", "issue": "4", "archive": "PMC", "archive_location": "PMC5493324", "abstract": "BACKGROUND: Carotenoids are a class of nutrients with antioxidant properties that have been purported to protect against cancer. However, the reported associations between carotenoids and prostate cancer have been heterogeneous and lacking data on interactions with nucleotide sequence variations and genomic biomarkers. OBJECTIVE: To examine the associations between carotenoid levels and the risk of high-grade prostate cancer, also considering antioxidant-related genes and tumor instability. METHODS: We measured plasma levels of carotenoids and genotyped 20 single nucleotide polymorphisms (SNP) in SOD1, SOD2, SOD3, XRCC1, and OGG1 among 559 men with non-metastatic prostate cancer undergoing radical prostatectomy. We performed copy number analysis in a subset of these men (n = 67) to study tumor instability assessed as Fraction of the Genome Altered (FGA). We examined associations between carotenoids, genotypes, tumor instability and risk of high-grade prostate cancer (Gleason grade $\geq 4 + 3$) using logistic and linear regression. RESULTS: Circulating carotenoid levels were inversely associated with the risk of high-grade prostate cancer; odds ratios (OR) and 95% confidence intervals (CI) comparing highest versus lowest quartiles were: 0.34 (95% CI: 0.18–0.66) for

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-carotene, 0.31 (95% CI: 0.15–0.63) for

β

-carotene, 0.55 (0.28–1.08) for lycopene and 0.37 (0.18–0.75) for total carotenoids. SNPs rs25489 in XRCC1, rs699473 in SOD3 and rs1052133 in OGG1 modified these associations for

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-carotene and lycopene, respectively ($P \leq 0.05$). The proportion of men with a high degree of FGA increased with Gleason Score ($P < 0.001$). Among men with Gleason score $\leq 3 + 4$, higher lycopene levels were associated with lower FGA ($P = 0.04$). CONCLUSION: Circulating carotenoids at diagnosis, particularly among men carrying specific somatic variations, were inversely associated with risk of high-grade prostate cancer. In exploratory analyses, higher lycopene level was associated with less genomic instability among men with low-grade disease which is novel and supports the hypothesis that lycopene may inhibit progression of prostate cancer early in its natural history.", "DOI": "10.1002/pros.23125", "ISSN": "0270-4137", "author":

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[{"family": "Ambrosini", "given": "G L"}, {"family": "Klerk", "given": "N H", "non-dropping-particle": "de"}, {"family": "Fritschi", "given": "L"}, {"family": "Mackerras", "given": "D"}, {"family": "Musk", "given": "B"}], "issued": [{"date-parts": [{"2007", 5, 22}]}], {"id": "773", "uris": [{"http://zotero.org/users/2724931/items/M8ZPITDZ"}], "uri": [{"http://zotero.org/users/2724931/items/M8ZPITDZ"}], "itemData": {"id": "773", "type": "article-journal", "title": "Prostate Cancer and Dietary Carotenoids", "container-title": "American Journal of Epidemiology", "page": "119-123", "volume": "151", "issue": "2", "abstract": "This population-based case-control study investigated associations between prostate cancer risk and dietary intake of the carotenoids

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-carotene and lycopene and their major plant food sources, including carrots, green leafy vegetables, and tomato-based foods. The study was carried out in Auckland, New Zealand, during 1996–1997 and recruited 317 prostate cancer cases and 480 controls. The authors found that dietary intake of

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-carotene and its main vegetable sources was largely unassociated with prostate cancer risk, whereas intake of lycopene and tomato-based foods was weakly associated with a reduced risk. These results suggest that in contrast to the findings regarding many types of cancers, vegetables rich in

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-carotene are not protective against prostate cancer. However, lycopene from tomato-based foods was found to be associated with a small reduction in risk. Am J Epidemiol 2000; 151:119–

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α
-carotene (OR = 0.85) and β -carotene (OR = 0.72), although the estimates were significant for carotene and β -carotene only. No meaningful associations emerged for nonprovitamin A carotenoids, such as lycopene (OR = 0.94) and lutein/zeaxanthin (OR = 0.91). No systematic heterogeneity was observed across strata of age, education and body mass index. Thus, our study supports the hypothesis of a weak protective effect of carotene, particularly β -carotene, on the risk of prostate cancer, while it indicates that other carotenoids, including lycopene, and retinol are not appreciably related to the risk of this neoplasm. ? 2004 Wiley-Liss, Inc.", "DOI": "10.1002/ijc.20486", "ISSN": "0020-7136", "journalAbbreviation": "International Journal of Cancer", "author": [{"family": "Bosetti", "given": "Cristina"}, {"family": "Talamini", "given": "Renato"}, {"family": "Montella", "given": "Maurizio"}, {"family": "Negri", "given": "Eva"}, {"family": "Conti", "given": "Ettore"}, {"family": "Franceschi", "given": "Silvia"}, {"family": "La Vecchia", "given": "Carlo"}], "issued": [{"date-parts": [{"2004", 7, 9}]}], {"id": "768", "uris": [{"http://zotero.org/users/2724931/items/84P4HPA6"}], "uri": [{"http://zotero.org/users/2724931/items/84P4HPA6"}], "itemData": {"id": "768", "type": "article-journal", "title": "Do dietary lycopene and other carotenoids protect against prostate cancer?", "container-title": "International Journal of Cancer", "page": "1010-1014", "volume": "113", "issue": "6", "abstract": "Abstract To determine whether dietary intake of lycopene and other carotenoids has an etiological association with prostate cancer, a case-control study was conducted in Hangzhou, southeast China during 2001–2002. The cases were 130 incident patients with histologically confirmed adenocarcinoma of the prostate. The controls were 274 hospital inpatients without prostate cancer or any other malignant diseases. Information on usual food consumption, including vegetables and fruits, was collected by face-to-face interviews using a structured food frequency questionnaire. The risks of prostate cancer for the intake of carotenoids and selected vegetables and fruits rich in carotenoids were assessed using multivariate logistic regression, adjusting for age, locality, education, income, body mass index, marital status, number of children, family history of prostate cancer, tea drinking, total fat and caloric intake. The prostate cancer risk declined with increasing consumption of lycopene,

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-carotene, β -carotene, β -cryptoxanthin, lutein and zeaxanthin. Intake of tomatoes, pumpkin, spinach, watermelon and citrus fruits were also inversely associated with the prostate cancer risk. The adjusted odds ratios for the highest versus the lowest quartiles of intake were 0.18 (95% CI: 0.08–0.41) for lycopene, 0.43 (95% CI: 0.21–0.85) for

α
-carotene, 0.34 (95% CI: 0.17–0.69) for β -carotene, 0.15 (95% CI: 0.06–0.34) for β -cryptoxanthin and 0.02 (95% CI: 0.01–0.10) for lutein and zeaxanthin. The corresponding dose-response relationships were also significant, suggesting that vegetables and fruits rich in lycopene and other carotenoids may be protective against prostate cancer. ? 2004 Wiley-Liss, Inc.", "DOI": "10.1002/ijc.20667", "ISSN": "0020-7136", "journalAbbreviation": "International Journal of Cancer", "author": [{"family": "Jian", "given": "Le"}, {"family": "Du", "given": "Chuan-Jun"}, {"family": "Lee", "given": "Andy H."}, {"family": "Binns", "given": "Colin W."}], "issued": [{"date-parts": [{"2004", 10, 28}]}], "schema": "https://github.com/citation-style-language/schema/raw/master/csl-citation.json"}]

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P

= 0.43)

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METHODS: We conducted a nested case-control study of serum antioxidant biomarkers (selenium, tocopherols, carotenoids, and retinol) and a urinary oxidation biomarker (15-isoprostane F(2t)) with risk of prostate cancer within the Multiethnic Cohort. Demographic, dietary, and other exposure information was collected by self-administered questionnaire in 1993-1996. We compared prediagnostic biomarker levels from 467 prostate cancer cases and 936 cancer free controls that were matched on several variables. Multivariate conditional logistic regression models were used to compute adjusted odds ratios (ORs) and 95% confidence intervals (CIs). RESULTS: We observed that there was no overall association of serum concentrations of antioxidants and urinary concentrations of 15-isoprostane F(2t) with risk of prostate cancer or risk of advanced prostate cancer. However, we did observe an inverse association for serum selenium only among African-American men (p trend = 0.02); men in the third tertile of selenium concentrations had a 41% lower risk (95% CI: 0.38-0.93) of prostate cancer when compared to men in the first tertile. CONCLUSIONS: Overall, our study found no association of serum antioxidants or 15-isoprostane F(2t) with the risk of prostate cancer. The observed inverse association of selenium with prostate cancer in African-Americans needs to be validated in other studies."},"DOI":"10.1007/s10552-009-9304-4","ISSN":"0957-5243","author":{"family":"Gill","given":"Jasmeet K"}, {"family":"Franke","given":"Adrian A"}, {"family":"Morris","given":"J Steven"}, {"family":"Cooney","given":"Robert V"}, {"family":"Wilkins","given":"Lynne R"}, {"family":"Le Marchand","given":"Loic"}, {"family":"Goodman","given":"Marc T"}, {"family":"Henderson","given":"Brian E"}, {"family":"Kolonel","given":"Laurence N"}],"issued":{"date-parts":["2009.9"]}}, {"id":767,"uris":["http://zotero.org/users/2724931/items/G2VXZNAR"],"uri":["http://zotero.org/users/2724931/items/G2VXZNAR"],"itemData":{"id":767,"type":"article-journal","title":"The Association between Lung and Prostate Cancer Risk, and Serum Micronutrients","container-title":"Cancer Epidemiology Biomarkers & Prevention","page":"518","volume":"12","issue":"6","abstract":"β -Carotene and Retinol Efficacy Trial is a nationwide chemoprevention trial that recruited 18,314 high-risk individuals to test the effect of supplemental β -carotene and retinol on lung cancer incidence. In this report, we conducted a prospective nested case-control study of the association between serum carotenoids, retinoids, and tocopherols on both lung and prostate cancer incidence. Prerandomization serum samples were selected from 278 lung cancer cases and 205 prostate cancer cases, and 483 controls matched by high-risk population, study center location, age, sex (lung cancer only), smoking status, and year of randomization. Carotenoids, retinoids, and tocopherols were analyzed by high-performance liquid chromatography. Endpoints were confirmed by pathology review (lung cancer) or review of the pathology report (prostate cancer). In the control-only population, there was a significant association between tobacco use and serum micronutrient concentration. Current smokers compared with former smokers had lower mean levels of all of the micronutrients tested with zeaxanthin, β -cryptoxanthin, α -carotene, α -tocopherol, retinol, and retinyl palmitate reaching statistical significance at P = 0.05. In the overall population, the mean serum concentrations of all of the micronutrients except γ -tocopherol were lower for lung cancer cases than controls. Statistically significant trends across quartiles were observed in lutein (P = 0.02), zeaxanthin (P = 0.02), and α -tocopherol (P = 0.03). The carotenoid findings in the overall population were because of the strong inverse association between serum micronutrients and lung cancer in females. Statistically significant odds ratios (ORs) comparing 4th to 1st quartiles in the female population were seen in lutein [OR, 0.31; confidence interval (CI), 0.13-0.75], zeaxanthin (OR, 0.31; CI, 0.12-0.77), and β -cryptoxanthin (OR, 0.34; CI, 0.14-0.81). For prostate cancer, mean serum concentrations were lower in cases for all of the nutrients except α -carotene. Only for α -tocopherol (P trend = 0.04) were the findings statistically significant. There was no statistically significant association between serum carotenoids and prostate cancer. Our findings provide additional support for the

association between physiological levels of dietary micronutrients and cancer incidence.", "journalAbbreviation": "Cancer Epidemiol Biomarkers Prev", "author": [{"family": "Goodman", "given": "Gary E."}, {"family": "Schaffer", "given": "Steven"}, {"family": "Omenn", "given": "Gilbert S."}, {"family": "Chen", "given": "Chu"}, {"family": "King", "given": "Irena"}], "issued": {"date-parts": [{"2003", 6, 1}]}, {"id": "775", "uris": ["http://zotero.org/users/2724931/items/6GDCVHDT"], "uri": ["http://zotero.org/users/2724931/items/6GDCVHDT"], "itemData": {"id": "775", "type": "article-journal", "title": "Serum Lycopene, Other Carotenoids, and Prostate Cancer Risk: a Nested Case-Control Study in the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial", "container-title": "Cancer Epidemiology Biomarkers & Prevention", "page": "962", "volume": "16", "issue": "5", "abstract": "Background: Reports from several studies have suggested that carotenoids, and in particular lycopene, could be prostate cancer-preventive agents. This has stimulated extensive laboratory and clinical research, as well as much commercial and public enthusiasm. However, the epidemiologic evidence remains inconclusive. Materials and Methods: We investigated the association between prediagnostic serum carotenoids (lycopene,

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-cryptoxanthin, lutein, and zeaxanthin) and risk of prostate cancer in the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial, a multicenter study designed to examine methods of early detection and risk factors for cancer. The study included 692 incident prostate cancer cases, diagnosed 1 to 8 years after study entry, including 270 aggressive cases, with regional or distant stage ($n = 90$) or Gleason score ≥ 7 ($n = 235$), and 844 randomly selected, matched controls. As study participants were selected from those who were assigned to annual standardized screening for prostate cancer, results are unlikely to be biased by differential screening, a circumstance that is difficult to attain under non-trial conditions. Results: No association was observed between serum lycopene and total prostate cancer [odds ratios (OR), 1.14; 95% confidence intervals (95% CI), 0.82-1.58 for highest versus lowest quintile; P for trend, 0.28] or aggressive prostate cancer (OR, 0.99; 95% CI, 0.62-1.57 for highest versus lowest quintile; P for trend, 0.433).

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-Carotene was associated with an increased risk of aggressive prostate cancer (OR, 1.67; 95% CI, 1.03-2.72 for highest versus lowest quintile; P for trend, 0.13); in particular, regional or distant stage disease (OR, 3.16; 95% CI, 1.37-7.31 for highest versus lowest quintile; P for trend, 0.02); other carotenoids were not associated with risk. Conclusion: In this large prospective study, high serum

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-carotene concentrations were associated with increased risk for aggressive, clinically relevant prostate cancer. Lycopene and other carotenoids were unrelated to prostate cancer. Consistent with other recent publications, these results suggest that lycopene or tomato-based regimens will not be effective for prostate cancer prevention.

(Cancer Epidemiol Biomarkers Prev 2007;16(5):962-8)", "DOI": "10.1158/1055-9965.EPI-06-0861", "journalAbbreviation": "Cancer Epidemiol Biomarkers Prev", "author":

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-carotene, and lycopene concentrations, and overall risk of prostate cancer diagnosis {odds ratio (highest versus lowest quintile; OR),

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-carotene: OR, 0.67 [95% confidence interval (CI), -0.40-1.09];

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-carotene: OR, 0.78 (95% CI, 0.48-1.25); lycopene: OR, 0.66 (95% CI, 0.38-1.13)}. The inverse association between plasma lycopene concentrations and prostate cancer risk was limited to participants who were 65 years or older (OR, 0.47; 95% CI, 0.23-0.98) and without a family history of prostate cancer (OR, 0.48; 95% CI, 0.26-0.89). Combining, older age and a negative family history provided similar results (OR, 0.43; 95% CI, 0.18-1.02). Inverse associations between

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-carotene and prostate cancer risk were also found among younger participants (<65 years of age; OR, 0.36; 95% CI, 0.14-0.91; P trend = 0.03). Combining dietary intake and plasma data confirmed our results. We found a statistically significant inverse association between higher plasma lycopene concentrations and lower risk of prostate cancer, which was restricted to older participants and those without a family history of prostate cancer. This observation suggests that tomato products may exhibit more potent protection against sporadic prostate cancer rather than those with a stronger familial or hereditary component. In addition, our findings also suggest that among younger men, diets rich in

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-carotene may also play a protective role in prostate carcinogenesis.", "DOI": "10.1158/1055-9965.EPI-03-0012", "journalAbbreviation": "Cancer Epidemiol Biomarkers Prev", "author": [{"family": "Wu", "given": "Kana"}, {"family": "Erdman", "given": "John W."}, {"family": "Schwartz", "given": "Steven J."}, {"family": "Platz", "given": "Elizabeth A."}, {"family": "Leitzmann", "given": "Michael"}, {"family": "Clinton", "given": "Steven K."}, {"family": "DeGroot", "given": "Valerie"}, {"family": "Willett", "given": "Walter C."}, {"family": "Giovannucci", "given": "Edward"}], "issued": {"date-parts": [{"2004", 2, 1}]}, {"id": "760", "uris": ["http://zotero.org/users/2724931/items/2YX9MMA"], "uri":

["http://zotero.org/users/2724931/items/2YX9MMBA"], "itemData": {"id": "760", "type": "article-journal", "title": "Retinol, carotenoids and the risk of prostate cancer: A case-control study from Italy", "container-title": "International Journal of Cancer", "page": "689-692", "volume": "112", "issue": "4", "abstract": "Abstract Several studies have evaluated the possible association between intakes of retinoids and carotenoids and the risk of prostate cancer, but the evidence is still inconsistent. Further, only a few studies have investigated the role of specific carotenoids other than β -carotene. We have thus considered the association between retinol and various carotenoids using data from a multicentric case-control study conducted in Italy between 1991 and 2002. This included 1,294 incident, histologically confirmed prostate cancer cases below age 75 years admitted to major teaching and general hospitals in the areas under study, and 1,451 controls below age 75 years selected among patients admitted to the same hospitals as cases for a wide spectrum of acute nonneoplastic conditions not related to long-term modifications of diet. Subjects' usual diet was investigated by means of a validated food-frequency questionnaire. Multivariate odds ratios and the corresponding 95% confidence intervals were estimated using unconditional logistic regression models. The risk of prostate cancer tended to decrease with increasing intake of retinol (OR = 0.79 for the highest versus the lowest quintile of intake), carotene (OR = 0.70),

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-carotene (OR = 0.85) and β -carotene (OR = 0.72), although the estimates were significant for carotene and β -carotene only. No meaningful associations emerged for nonprovitamin A carotenoids, such as lycopene (OR = 0.94) and lutein/zeaxanthin (OR = 0.91). No systematic heterogeneity was observed across strata of age, education and body mass index. Thus, our study supports the hypothesis of a weak protective effect of carotene, particularly β -carotene, on the risk of prostate cancer, while it indicates that other carotenoids, including lycopene, and retinol are not appreciably related to the risk of this neoplasm. ? 2004 Wiley-Liss, Inc., "DOI": "10.1002/ijc.20486", "ISSN": "0020-7136", "journalAbbreviation": "International Journal of Cancer", "author": [{"family": "Bosetti", "given": "Cristina"}, {"family": "Talamini", "given": "Renato"}, {"family": "Montella", "given": "Maurizio"}, {"family": "Negri", "given": "Eva"}, {"family": "Conti", "given": "Ettore"}, {"family": "Franceschi", "given": "Silvia"}, {"family": "La Vecchia", "given": "Carlo"}], "issued": {"date-parts": [{"2004", "7", "9"}]}, {"id": "768", "uris":

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-carotene, β -carotene, β -cryptoxanthin, lutein and zeaxanthin. Intake of tomatoes, pumpkin, spinach, watermelon and citrus fruits were also inversely associated with the prostate cancer risk. The adjusted odds ratios for the highest versus the lowest quartiles of intake were 0.18 (95% CI: 0.08-0.41) for lycopene, 0.43 (95% CI: 0.21-0.85) for

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-carotene, 0.34 (95% CI: 0.17-0.69) for β -carotene, 0.15 (95% CI: 0.06-0.34) for β -cryptoxanthin and 0.02 (95% CI: 0.01-0.10) for lutein and zeaxanthin. The corresponding dose-response relationships were also significant, suggesting that vegetables and fruits rich in lycopene and other carotenoids may be protective against prostate cancer. ? 2004 Wiley-Liss, Inc., "DOI": "10.1002/ijc.20667", "ISSN": "0020-7136", "journalAbbreviation": "International Journal of Cancer", "author": [{"family": "Jian", "given": "Le"}, {"family": "Du", "given": "Chuan-Jun"}, {"family": "Lee", "given": "Andy H."}, {"family": "Binns", "given": "Colin W."}], "issued": {"date-parts": [{"2004", "10", "28"}]}, "schema": "https://github.com/citation-style-language/schema/raw/master/csl-citation.json"}
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0.86 [0.64-1.15]

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P

= 0.31)

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1171", "volume": "20", "issue": "7", "archive": "PMC", "archive_location": "PMC2725220", "abstract": "OBJECTIVE:

We examine the association of antioxidants and 15-isoprostane F(2t) with risk of prostate cancer. **METHODS:** We conducted a nested case-control study of serum antioxidant biomarkers (selenium, tocopherols, carotenoids, and retinol) and a urinary oxidation biomarker (15-isoprostane F(2t)) with risk of prostate cancer within the Multiethnic Cohort. Demographic, dietary, and other exposure information was collected by self-administered questionnaire in 1993–1996. We compared prediagnostic biomarker levels from 467 prostate cancer cases and 936 cancer free controls that were matched on several variables. Multivariate conditional logistic regression models were used to compute adjusted odds ratios (ORs) and 95% confidence intervals (CIs). **RESULTS:** We observed that there was no overall association of serum concentrations of antioxidants and urinary concentrations of 15-isoprostane F(2t) with risk of prostate cancer or risk of advanced prostate cancer. However, we did observe an inverse association for serum selenium only among African-American men (p trend = 0.02); men in the third tertile of selenium concentrations had a 41% lower risk (95% CI: 0.38–0.93) of prostate cancer when compared to men in the first tertile. **CONCLUSIONS:** Overall, our study found no association of serum antioxidants or 15-isoprostane F(2t) with the risk of prostate cancer. The observed inverse association of selenium with prostate cancer in African-Americans needs to be validated in other studies.,"DOI":"10.1007/s10552-009-9304-4","ISSN":"0957-5243","author":[{"family":"Gill","given":"Jasmeet K"}, {"family":"Franke","given":"Adrian A"}, {"family":"Morris","given":"J Steven"}, {"family":"Cooney","given":"Robert V"}, {"family":"Wilkins","given":"Lynne R"}, {"family":"Le Marchand","given":"Loic"}, {"family":"Goodman","given":"Marc T"}, {"family":"Henderson","given":"Brian E"}, {"family":"Kolonel","given":"Laurence N"}],"issued":{"date-parts":["2009",9]}},{id:"767","uris":["http://zotero.org/users/2724931/items/G2VXZNR"],"uri":["http://zotero.org/users/2724931/items/G2VXZNR"],"itemData":{"id":767,"type":"article-journal","title":"The Association between Lung and Prostate Cancer Risk, and Serum Micronutrients","container-title":"Cancer Epidemiology Biomarkers & Prevention","page":518,"volume":12,"issue":6,"abstract":"

β
-Carotene and Retinol Efficacy Trial is a nationwide chemoprevention trial that recruited 18,314 high-risk individuals to test the effect of supplemental

β
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β
-cryptoxanthin,

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-carotene,

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-tocopherol, retinol, and retinyl palmitate reaching statistical significance at $P = 0.05$. In the overall population, the mean serum concentrations of all of the micronutrients except

γ
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α
-tocopherol ($P = 0.03$). The carotenoid findings in the overall population were because of the strong inverse association between serum micronutrients and lung cancer in females. Statistically significant odds ratios (ORs) comparing 4th to 1st quartiles in the female population were seen in lutein [OR, 0.31; confidence interval (CI), 0.13–0.75], zeaxanthin (OR, 0.31; CI, 0.12–0.77), and

β
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α
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α
-tocopherol (P trend = 0.04) were the findings statistically significant. There was no statistically significant association between serum carotenoids and prostate cancer. Our findings provide additional support for the association between physiological levels of dietary micronutrients and cancer incidence.,"journalAbbreviation":"Cancer Epidemiol Biomarkers Prev","author":[{"family":"Goodman","given":"Gary E."}, {"family":"Schaffer","given":"Steven"}, {"family":"Omenn","given":"Gilbert S."}, {"family":"Chen","given":"Chu"}, {"family":"King","given":"Irena"}],"issued":{"date-parts":["2003",6,1]}},{id:"775","uris":["http://zotero.org/users/2724931/items/6GDCVHDT"],"uri":["http://zotero.org/users/2724931/items/6GDCVHDT"],"itemData":{"id":775,"type":"article-journal","title":"Serum Lycopene, Other Carotenoids, and Prostate Cancer Risk: a Nested Case-Control Study in the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial","container-title":"Cancer Epidemiology Biomarkers & Prevention","page":962,"volume":16,"issue":5,"abstract":"Background: Reports from several studies have suggested that carotenoids, and in particular lycopene, could be prostate cancer-preventive agents. This has stimulated extensive laboratory and clinical research, as well as much commercial and public enthusiasm. However, the epidemiologic evidence remains inconclusive. Materials and Methods: We investigated the association between prediagnostic serum carotenoids (lycopene,

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selected, matched controls. As study participants were selected from those who were assigned to annual standardized screening for prostate cancer, results are unlikely to be biased by differential screening, a circumstance that is difficult to attain under non-trial conditions. Results: No association was observed between serum lycopene and total prostate cancer [odds ratios (OR), 1.14; 95% confidence intervals (95% CI), 0.82-1.58 for highest versus lowest quintile; P for trend, 0.28] or aggressive prostate cancer (OR, 0.99; 95% CI, 0.62-1.57 for highest versus lowest quintile; P for trend, 0.433).

β

-Carotene was associated with an increased risk of aggressive prostate cancer (OR, 1.67; 95% CI, 1.03-2.72 for highest versus lowest quintile; P for trend, 0.13); in particular, regional or distant stage disease (OR, 3.16; 95% CI, 1.37-7.31 for highest versus lowest quintile; P for trend, 0.02); other carotenoids were not associated with risk.

Conclusion: In this large prospective study, high serum

β

-carotene concentrations were associated with increased risk for aggressive, clinically relevant prostate cancer. Lycopene and other carotenoids were unrelated to prostate cancer. Consistent with other recent publications, these results suggest that lycopene or tomato-based regimens will not be effective for prostate cancer prevention. (Cancer Epidemiol Biomarkers Prev 2007;16(5):962-8),"DOI":"10.1158/1055-9965.EPI-06-0861","journalAbbreviation":"Cancer Epidemiol Biomarkers Prev","author":[{"family":"Peters","given":"Ulrike"}, {"family":"Leitzmann","given":"Michael F."}, {"family":"Chatterjee","given":"Nilanjan"}, {"family":"Wang","given":"Yinghui"}, {"family":"Albanes","given":"Demetrius"}, {"family":"Germann","given":"Edward P."}, {"family":"Friesen","given":"Marlin D."}, {"family":"Riboli","given":"Elio"}, {"family":"Hayes","given":"Richard B."}], "issued":{"date-parts":[[2007,5,1]]}}, {"id":"776","uris":["http://zotero.org/users/2724931/items/QIHK2VR"],"uri":["http://zotero.org/users/2724931/items/QIHK2VR"],"itemData":{"id":"776","type":"article-journal","title":"Plasma and Dietary Carotenoids, and the Risk of Prostate Cancer","container-title":"Cancer Epidemiology Biomarkers & Prevention","page":"260","volume":"13","issue":"2","abstract":"The association between plasma carotenoids and prostate cancer risk was investigated in a case-control study nested within the prospective Health Professionals Follow-up Study. We matched 450 incident prostate cancer cases diagnosed from 1993-1998 to 450 controls by age, time, and year of blood donation. Modest inverse, but not statistically significant, associations were observed among plasma

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-carotene,

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-carotene, and lycopene concentrations, and overall risk of prostate cancer diagnosis {odds ratio (highest versus lowest quintile; OR),

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-carotene: OR, 0.67 [95% confidence interval (CI), -0.40-1.09];

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-carotene: OR, 0.78 (95% CI, 0.48-1.25); lycopene: OR, 0.66 (95% CI, 0.38-1.13)). The inverse association between plasma lycopene concentrations and prostate cancer risk was limited to participants who were 65 years or older (OR, 0.47; 95% CI, 0.23-0.98) and without a family history of prostate cancer (OR, 0.48; 95% CI, 0.26-0.89). Combining, older age and a negative family history provided similar results (OR, 0.43; 95% CI, 0.18-1.02). Inverse associations between

β

-carotene and prostate cancer risk were also found among younger participants (<65 years of age; OR, 0.36; 95% CI, 0.14-0.91; P trend = 0.03). Combining dietary intake and plasma data confirmed our results. We found a statistically significant inverse association between higher plasma lycopene concentrations and lower risk of prostate cancer, which was restricted to older participants and those without a family history of prostate cancer. This observation suggests that tomato products may exhibit more potent protection against sporadic prostate cancer rather than those with a stronger familial or hereditary component. In addition, our findings also suggest that among younger men, diets rich in

β

-carotene may also play a protective role in prostate carcinogenesis."DOI":"10.1158/1055-9965.EPI-03-0012","journalAbbreviation":"Cancer Epidemiol Biomarkers Prev","author":[{"family":"Wu","given":"Kana"}, {"family":"Erdman","given":"John W."}, {"family":"Schwartz","given":"Steven J."}, {"family":"Platz","given":"Elizabeth A."}, {"family":"Leitzmann","given":"Michael"}, {"family":"Clinton","given":"Steven K."}, {"family":"DeGroot","given":"Valerie"}, {"family":"Willett","given":"Walter C."}, {"family":"Giovannucci","given":"Edward"}], "issued":{"date-parts":[[2004,2,1]]}}, {"id":"760","uris":["http://zotero.org/users/2724931/items/2YX9MMBA"],"uri":["http://zotero.org/users/2724931/items/2YX9MMBA"],"itemData":{"id":"760","type":"article-journal","title":"Retinol, carotenoids and the risk of prostate cancer: A case-control study from Italy","container-title":"International Journal of Cancer","page":"689-692","volume":"112","issue":"4","abstract":"Abstract Several studies have evaluated the possible association between intakes of retinoids and carotenoids and the risk of prostate cancer, but the evidence is still inconsistent. Further, only a few studies have investigated the role of specific carotenoids other than β -carotene. We have thus considered the association between retinol and various carotenoids using data from a multicentric case-control study conducted in Italy between 1991 and 2002. This included 1,294 incident, histologically confirmed prostate cancer cases below age 75 years admitted to major teaching and general hospitals in the areas under study, and 1,451 controls below age 75 years selected among patients admitted to the same hospitals as cases for a wide spectrum of acute nonneoplastic conditions not related to long-term modifications of diet. Subjects' usual diet was investigated by means of a validated food-frequency questionnaire. Multivariate odds ratios and the corresponding 95% confidence intervals were estimated using unconditional logistic regression models. The risk of prostate cancer tended to decrease with increasing intake of retinol (OR = 0.79 for the highest versus the lowest quintile of intake), carotene (OR = 0.70),

α

-carotene (OR = 0.85) and β -carotene (OR = 0.72), although the estimates were significant for carotene and β -carotene only. No meaningful associations emerged for nonprovitamin A carotenoids, such as lycopene (OR = 0.94) and lutein/zeaxanthin (OR = 0.91). No systematic heterogeneity was observed across strata of age, education and body mass index. Thus, our study supports the hypothesis of a weak protective effect of carotene, particularly β -carotene, on the risk of prostate cancer, while it indicates that other carotenoids, including lycopene, and retinol are not appreciably related to the risk of this neoplasm. © 2004 Wiley-Liss, Inc."DOI":"10.1002/ijc.20486","ISSN":"0020-7136","journalAbbreviation":"International Journal of Cancer","author":[{"family":"Bosetti","given":"Cristina"}, {"family":"Talamini","given":"Renato"},

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dietary lycopene and other carotenoids protect against prostate cancer?", "container-title": "International Journal of
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of lycopene and other carotenoids has an etiological association with prostate cancer, a case-control study was
conducted in Hangzhou, southeast China during 2001-2002. The cases were 130 incident patients with
histologically confirmed adenocarcinoma of the prostate. The controls were 274 hospital inpatients without
prostate cancer or any other malignant diseases. Information on usual food consumption, including vegetables and
fruits, was collected by face-to-face interviews using a structured food frequency questionnaire. The risks of
prostate cancer for the intake of carotenoids and selected vegetables and fruits rich in carotenoids were assessed
using multivariate logistic regression, adjusting for age, locality, education, income, body mass index, marital
status, number of children, family history of prostate cancer, tea drinking, total fat and caloric intake. The prostate
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α
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7136", "journalAbbreviation": "International Journal of Cancer", "author": [{"family": "Jian", "given": "Le"},
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incidence.", "journalAbbreviation": "Cancer Epidemiol Biomarkers Prev", "author": [{"family": "Goodman", "given": "Gary E."}, {"family": "Schaffer", "given": "Steven"}, {"family": "Omenn", "given": "Gilbert S."}, {"family": "Chen", "given": "Chu"}, {"family": "King", "given": "Irena"}], "issued": {"date-parts": [{"2003", 6, 1}]}, {"id": "775", "uris": [{"http://zotero.org/users/2724931/items/6GDCVHDT"}, {"uri": [{"http://zotero.org/users/2724931/items/6GDCVHDT"}, {"itemData": {"id": "775", "type": "article-journal", "title": "Serum Lycopene, Other Carotenoids, and Prostate Cancer Risk: a Nested Case-Control Study in the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial", "container-title": "Cancer Epidemiology Biomarkers & Prevention", "page": "962", "volume": "16", "issue": "5", "abstract": "Background: Reports from several studies have suggested that carotenoids, and in particular lycopene, could be prostate cancer-preventive agents. This has stimulated extensive laboratory and clinical research, as well as much commercial and public enthusiasm. However, the epidemiologic evidence remains inconclusive. Materials and Methods: We investigated the association between prediagnostic serum carotenoids (lycopene,

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-carotene and prostate cancer risk were also found among younger participants (<65 years of age; OR, 0.36; 95% CI, 0.14–0.91; Ptrend = 0.03). Combining dietary intake and plasma data confirmed our results. We found a statistically significant inverse association between higher plasma lycopene concentrations and lower risk of prostate cancer, which was restricted to older participants and those without a family history of prostate cancer. This observation suggests that tomato products may exhibit more potent protection against sporadic prostate

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β -carotene may also play a protective role in prostate carcinogenesis.", "DOI": "10.1158/1055-9965.EPI-03-0012", "journalAbbreviation": "Cancer Epidemiol Biomarkers Prev", "author": [{"family": "Wu", "given": "Kana"}, {"family": "Erdman", "given": "John W."}, {"family": "Schwartz", "given": "Steven J."}, {"family": "Platz", "given": "Elizabeth A."}, {"family": "Leitzmann", "given": "Michael"}, {"family": "Clinton", "given": "Steven K."}, {"family": "DeGroot", "given": "Valerie"}, {"family": "Willett", "given": "Walter C."}, {"family": "Giovannucci", "given": "Edward"}], "issued": {"date-parts": [{"2004", 2, 1}]}, {"id": "772", "uris": [{"http://zotero.org/users/2724931/items/Z88XYJCK"}], "uri": [{"http://zotero.org/users/2724931/items/Z88XYJCK"}], "itemData": {"id": "772", "type": "article-journal", "title": "Associations Between Circulating Carotenoids, Genomic Instability and the Risk of High-Grade Prostate Cancer", "container-title": "The Prostate", "page": "339-348", "volume": "76", "issue": "4", "archive": "PMC", "archive_location": "PMC5493324", "abstract": "BACKGROUND: Carotenoids are a class of nutrients with antioxidant properties that have been purported to protect against cancer. However, the reported associations between carotenoids and prostate cancer have been heterogeneous and lacking data on interactions with nucleotide sequence variations and genomic biomarkers. OBJECTIVE: To examine the associations between carotenoid levels and the risk of high-grade prostate cancer, also considering antioxidant-related genes and tumor instability. METHODS: We measured plasma levels of carotenoids and genotyped 20 single nucleotide polymorphisms (SNP) in SOD1, SOD2, SOD3, XRCC1, and OGG1 among 559 men with non-metastatic prostate cancer undergoing radical prostatectomy. We performed copy number analysis in a subset of these men (n = 67) to study tumor instability assessed as Fraction of the Genome Altered (FGA). We examined associations between carotenoids, genotypes, tumor instability and risk of high-grade prostate cancer (Gleason grade $\geq 4 + 3$) using logistic and linear regression. RESULTS: Circulating carotenoid levels were inversely associated with the risk of high-grade prostate cancer; odds ratios (OR) and 95% confidence intervals (CI) comparing highest versus lowest quartiles were: 0.34 (95% CI: 0.18–0.66) for

α -carotene, 0.31 (95% CI: 0.15–0.63) for

β -carotene, 0.55 (0.28–1.08) for lycopene and 0.37 (0.18–0.75) for total carotenoids. SNPs rs25489 in XRCC1, rs699473 in SOD3 and rs1052133 in OGG1 modified these associations for

α -carotene,

β -carotene and lycopene, respectively ($P \leq 0.05$). The proportion of men with a high degree of FGA increased with Gleason Score ($P < 0.001$). Among men with Gleason score $\leq 3 + 4$, higher lycopene levels were associated with lower FGA ($P = 0.04$). CONCLUSION: Circulating carotenoids at diagnosis, particularly among men carrying specific somatic variations, were inversely associated with risk of high-grade prostate cancer. In exploratory analyses, higher lycopene level was associated with less genomic instability among men with low-grade disease which is novel and supports the hypothesis that lycopene may inhibit progression of prostate cancer early in its natural history.", "DOI": "10.1002/pros.23125", "ISSN": "0270-4137", "author": [{"family": "Nordström", "given": "Tobias"}, {"family": "Van Blarigan", "given": "Erin L"}, {"family": "Ngo", "given": "Vy"}, {"family": "Roy", "given": "Ritu"}, {"family": "Weinberg", "given": "Vivian"}, {"family": "Song", "given": "Xiaoling"}, {"family": "Simko", "given": "Jeffrey"}, {"family": "Carroll", "given": "Peter R"}, {"family": "Chan", "given": "June M"}, {"family": "Paris", "given": "Pamela L"}], "issued": {"date-parts": [{"2016", 3, 1}]}, {"id": "760", "uris": [{"http://zotero.org/users/2724931/items/2YX9MMBA"}], "uri": [{"http://zotero.org/users/2724931/items/2YX9MMBA"}], "itemData": {"id": "760", "type": "article-journal", "title": "Retinol, carotenoids and the risk of prostate cancer: A case-control study from Italy", "container-title": "International Journal of Cancer", "page": "689-692", "volume": "112", "issue": "4", "abstract": "Abstract Several studies have evaluated the possible association between intakes of retinoids and carotenoids and the risk of prostate cancer, but the evidence is still inconsistent. Further, only a few studies have investigated the role of specific carotenoids other than β -carotene. We have thus considered the association between retinol and various carotenoids using data from a multicentric case-control study conducted in Italy between 1991 and 2002. This included 1,294 incident, histologically confirmed prostate cancer cases below age 75 years admitted to major teaching and general hospitals in the areas under study, and 1,451 controls below age 75 years selected among patients admitted to the same hospitals as cases for a wide spectrum of acute nonneoplastic conditions not related to long-term modifications of diet. Subjects' usual diet was investigated by means of a validated food-frequency questionnaire. Multivariate odds ratios and the corresponding 95% confidence intervals were estimated using unconditional logistic regression models. The risk of prostate cancer tended to decrease with increasing intake of retinol (OR = 0.79 for the highest versus the lowest quintile of intake), carotene (OR = 0.70),

α -carotene (OR = 0.85) and β -carotene (OR = 0.72), although the estimates were significant for carotene and β -carotene only. No meaningful associations emerged for nonprovitamin A carotenoids, such as lycopene (OR = 0.94) and lutein/zeaxanthin (OR = 0.91). No systematic heterogeneity was observed across strata of age, education and body mass index. Thus, our study supports the hypothesis of a weak protective effect of carotene, particularly β -carotene, on the risk of prostate cancer, while it indicates that other carotenoids, including lycopene, and retinol are not appreciably related to the risk of this neoplasm. © 2004 Wiley-Liss, Inc.", "DOI": "10.1002/ijc.20486", "ISSN": "0020-7136", "journalAbbreviation": "International Journal of Cancer", "author": [{"family": "Bosetti", "given": "Cristina"}, {"family": "Talamini", "given": "Renato"}, {"family": "Montella", "given": "Maurizio"}, {"family": "Negri", "given": "Eva"}, {"family": "Conti", "given": "Ettore"}, {"family": "Franceschi", "given": "Silvia"}, {"family": "La Vecchia", "given": "Carlo"}], "issued": {"date-parts": [{"2004", 7, 9}]}, {"id": "768", "uris": [{"http://zotero.org/users/2724931/items/84P4HPA6"}], "uri": [{"http://zotero.org/users/2724931/items/84P4HPA6"}], "itemData": {"id": "768", "type": "article-journal", "title": "Do dietary lycopene and other carotenoids protect against prostate cancer?", "container-title": "International Journal of Cancer", "page": "1010-1014", "volume": "113", "issue": "6", "abstract": "Abstract To determine whether dietary intake of lycopene and other carotenoids has an etiological association with prostate cancer, a case-control study was conducted in Hangzhou, southeast China during 2001-2002. The cases were 130 incident patients with histologically confirmed adenocarcinoma of the prostate. The controls were 274 hospital inpatients without prostate cancer or any other malignant diseases. Information on usual food consumption, including vegetables and fruits, was collected by face-to-face interviews using a structured food frequency questionnaire. The risks of prostate cancer for the intake of carotenoids and selected vegetables and fruits rich in carotenoids were assessed

using multivariate logistic regression, adjusting for age, locality, education, income, body mass index, marital status, number of children, family history of prostate cancer, tea drinking, total fat and caloric intake. The prostate cancer risk declined with increasing consumption of lycopene,

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-carotene, β -carotene, β -cryptoxanthin, lutein and zeaxanthin. Intake of tomatoes, pumpkin, spinach, watermelon and citrus fruits were also inversely associated with the prostate cancer risk. The adjusted odds ratios for the highest versus the lowest quartiles of intake were 0.18 (95% CI: 0.08-0.41) for lycopene, 0.43 (95% CI: 0.21-0.85) for

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-carotene, 0.34 (95% CI: 0.17-0.69) for β -carotene, 0.15 (95% CI: 0.06-0.34) for β -cryptoxanthin and 0.02 (95% CI: 0.01-0.10) for lutein and zeaxanthin. The corresponding dose-response relationships were also significant, suggesting that vegetables and fruits rich in lycopene and other carotenoids may be protective against prostate cancer. © 2004 Wiley-Liss, Inc., "DOI": "10.1002/ijc.20667", "ISSN": "0020-7136", "journalAbbreviation": "International Journal of Cancer", "author": [{"family": "Jian", "given": "Le"}, {"family": "Du", "given": "Chuan-Jun"}, {"family": "Lee", "given": "Andy H."}, {"family": "Binns", "given": "Colin W."}], "issued": {"date-parts": [{"2004", "10", "28"}]}, "schema": "https://github.com/citation-style-language/schema/raw/master/csl-citation.json"}
23, 24, 26, 28, 32, 34

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RE

0.80 [0.60-1.07]

1.47

(

P

= 0.14)

59

0.07

12.16, df=5

(

P

= 0.03)

NA

NA

not applicable

, OR

odds ratio

, RE

random effects

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Table 3:

Subgroup analysis

s

results

of the association between Lycopene and prostate cancer

Subgroups

No

of studies

(

No

of datasets)

References

Model

OR [95% CI]

Z- test

Heterogeneity

I² (%)

T²

X²

All studies

11 (15)

[

ADDN ZOTERO_ITEM CSL_CITATION {"citationID":"w08JGPiG","properties":{"formattedCitation":"\supersub{22-24,26-29,31-34}","noteIndex":0},"citationItems":[{"id":"764","uris":["http://zotero.org/users/2724931/items/KKJLTJHE"],"uri":["http://zotero.org/users/2724931/items/KKJLTJHE"],"itemData":{"id":"764","type":"article-journal","title":"Association of selenium, tocopherols, carotenoids, retinol, and 15-isoprostane F(2t) in serum or urine with prostate cancer risk: the multiethnic cohort","container-title":"Cancer causes & control : CCC","page":"1161-1171","volume":"20","issue":"7","archive":"PMC","archive_location":"PMC2725220","abstract":"OBJECTIVE: We examine the association of antioxidants and 15-isoprostane F(2t) with risk of prostate cancer. METHODS: We conducted a nested case-control study of serum antioxidant biomarkers (selenium, tocopherols, carotenoids, and retinol) and a urinary oxidation biomarker (15-isoprostane F(2t)) with risk of prostate cancer within the Multiethnic Cohort. Demographic, dietary, and other exposure information was collected by self-administered questionnaire in 1993-1996. We compared prediagnostic biomarker levels from 467 prostate cancer cases and 936 cancer free controls that were matched on several variables. Multivariate conditional logistic regression models were used to compute adjusted odds ratios (ORs) and 95% confidence intervals (CIs). RESULTS: We observed that there was no overall association of serum concentrations of antioxidants and urinary concentrations of 15-isoprostane F(2t) with risk of prostate cancer or risk of advanced prostate cancer. However, we did observe an inverse association for serum selenium only among African-American men (p trend = 0.02); men in the third tertile of selenium concentrations had a 41% lower risk (95% CI: 0.38-0.93) of prostate cancer when compared to men in the first tertile. CONCLUSIONS: Overall, our study found no association of serum antioxidants or 15-isoprostane F(2t) with the risk of prostate cancer. The observed inverse association of selenium with prostate

cancer in African-Americans needs to be validated in other studies.", "DOI": "10.1007/s10552-009-9304-4", "ISSN": "0957-5243", "author": [{"family": "Gill", "given": "Jasmeet K"}, {"family": "Franke", "given": "Adrian A"}, {"family": "Morris", "given": "J Steven"}, {"family": "Cooney", "given": "Robert V"}, {"family": "Wilkens", "given": "Lynne R"}, {"family": "Le Marchand", "given": "Loic"}, {"family": "Goodman", "given": "Marc T"}, {"family": "Henderson", "given": "Brian E"}, {"family": "Kolonel", "given": "Laurence N"}], "issued": {"date-parts": [{"2009", 9]}]}, {"id": "767", "uris": ["http://zotero.org/users/2724931/items/G2VXZNR"], "uri": ["http://zotero.org/users/2724931/items/G2VXZNR"], "itemData": {"id": "767", "type": "article-journal", "title": "The Association between Lung and Prostate Cancer Risk, and Serum Micronutrients", "container-title": "Cancer Epidemiology Biomarkers & Prevention", "page": "518", "volume": "12", "issue": "6", "abstract": "\u03b2

-Carotene and Retinol Efficacy Trial is a nationwide chemoprevention trial that recruited 18,314 high-risk individuals to test the effect of supplemental

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-carotene and retinol on lung cancer incidence. In this report, we conducted a prospective nested case-control study of the association between serum carotenoids, retinoids, and tocopherols on both lung and prostate cancer incidence. Prerandomization serum samples were selected from 278 lung cancer cases and 205 prostate cancer cases, and 483 controls matched by high-risk population, study center location, age, sex (lung cancer only), smoking status, and year of randomization. Carotenoids, retinoids, and tocopherols were analyzed by high-performance liquid chromatography. Endpoints were confirmed by pathology review (lung cancer) or review of the pathology report (prostate cancer). In the control-only population, there was a significant association between tobacco use and serum micronutrient concentration. Current smokers compared with former smokers had lower mean levels of all of the micronutrients tested with zeaxanthin,

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-cryptoxanthin,

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-carotene,

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-tocopherol, retinol, and retinyl palmitate reaching statistical significance at $P = 0.05$. In the overall population, the mean serum concentrations of all of the micronutrients except

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-tocopherol were lower for lung cancer cases than controls. Statistically significant trends across quartiles were observed in lutein ($P = 0.02$), zeaxanthin ($P = 0.02$), and

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-tocopherol ($P = 0.03$). The carotenoid findings in the overall population were because of the strong inverse association between serum micronutrients and lung cancer in females. Statistically significant odds ratios (ORs) comparing 4th to 1st quartiles in the female population were seen in lutein [OR, 0.31; confidence interval (CI), 0.13–0.75], zeaxanthin (OR, 0.31; CI, 0.12–0.77), and

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-cryptoxanthin (OR, 0.34; CI, 0.14–0.81). For prostate cancer, mean serum concentrations were lower in cases for all of the nutrients except

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-carotene. Only for

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-tocopherol ($P_{trend} = 0.04$) were the findings statistically significant. There was no statistically significant association between serum carotenoids and prostate cancer. Our findings provide additional support for the association between physiological levels of dietary micronutrients and cancer incidence.", "journalAbbreviation": "Cancer Epidemiol Biomarkers Prev", "author": [{"family": "Goodman", "given": "Gary E."}, {"family": "Schaffer", "given": "Steven"}, {"family": "Omenn", "given": "Gilbert S."}, {"family": "Chen", "given": "Chu"}, {"family": "King", "given": "Irena"}], "issued": {"date-parts": [{"2003", 6, 1]}]}, {"id": "775", "uris": ["http://zotero.org/users/2724931/items/6GDCVHDT"], "uri": ["http://zotero.org/users/2724931/items/6GDCVHDT"], "itemData": {"id": "775", "type": "article-journal", "title": "Serum Lycopene, Other Carotenoids, and Prostate Cancer Risk: a Nested Case-Control Study in the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial", "container-title": "Cancer Epidemiology Biomarkers & Prevention", "page": "962", "volume": "16", "issue": "5", "abstract": "Background: Reports from several studies have suggested that carotenoids, and in particular lycopene, could be prostate cancer-preventive agents. This has stimulated extensive laboratory and clinical research, as well as much commercial and public enthusiasm. However, the epidemiologic evidence remains inconclusive. Materials and Methods: We investigated the association between prediagnostic serum carotenoids (lycopene,

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-carotene,

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-carotene,

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-cryptoxanthin, lutein, and zeaxanthin) and risk of prostate cancer in the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial, a multicenter study designed to examine methods of early detection and risk factors for cancer. The study included 692 incident prostate cancer cases, diagnosed 1 to 8 years after study entry, including 270 aggressive cases, with regional or distant stage ($n = 90$) or Gleason score ≥ 7 ($n = 235$), and 844 randomly selected, matched controls. As study participants were selected from those who were assigned to annual standardized screening for prostate cancer, results are unlikely to be biased by differential screening, a circumstance that is difficult to attain under non-trial conditions. Results: No association was observed between serum lycopene and total prostate cancer [odds ratios (OR), 1.14; 95% confidence intervals (95% CI), 0.82–1.58 for highest versus lowest quintile; P for trend, 0.28] or aggressive prostate cancer (OR, 0.99; 95% CI, 0.62–1.57 for highest versus lowest quintile; P for trend, 0.433).

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-Carotene was associated with an increased risk of aggressive prostate cancer (OR, 1.67; 95% CI, 1.03–2.72 for highest versus lowest quintile; P for trend, 0.13); in particular, regional or distant stage disease (OR, 3.16; 95% CI, 1.37–7.31 for highest versus lowest quintile; P for trend, 0.02); other carotenoids were not associated with risk. Conclusion: In this large prospective study, high serum

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-carotene concentrations were associated with increased risk for aggressive, clinically relevant prostate cancer. Lycopene and other carotenoids were unrelated to prostate cancer. Consistent with other recent publications, these results suggest that lycopene or tomato-based regimens will not be effective for prostate cancer prevention. (Cancer Epidemiol Biomarkers Prev 2007;16(5):962–8)", "DOI": "10.1158/1055-9965.EPI-06-0861", "journalAbbreviation": "Cancer Epidemiol Biomarkers Prev", "author": [{"family": "Peters", "given": "Ulrike"}, {"family": "Leitzmann", "given": "Michael F."}, {"family": "Chatterjee", "given": "Nilanjan"}, {"family": "Wang", "given": "Yinghui"}, {"family": "Albanes", "given": "Demetrius"}, {"family": "Germann", "given": "Edward P."}, {"family": "Friesen", "given": "Marlin D."}, {"family": "Riboli", "given": "Elio"}, {"family": "Hayes", "given": "Richard B."}], "issued": {"date-parts": [{"2007", 5, 1}]}, {"id": "776", "uris": [{"http://zotero.org/users/2724931/items/QIHKN2VR"}], "uri": [{"http://zotero.org/users/2724931/items/QIHKN2VR"}], "itemData": {"id": "776", "type": "article-journal", "title": "Plasma and Dietary Carotenoids, and the Risk of Prostate Cancer", "container-title": "Cancer Epidemiology Biomarkers & Prevention", "page": "260", "volume": "13", "issue": "2", "abstract": "The association between plasma carotenoids and prostate cancer risk was investigated in a case-control study nested within the prospective Health Professionals Follow-up Study. We matched 450 incident prostate cancer cases diagnosed from 1993–1998 to 450 controls by age, time, month, and year of blood donation. Modest inverse, but not statistically significant, associations were observed among plasma

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-carotene, and lycopene concentrations, and overall risk of prostate cancer diagnosis {odds ratio (highest versus lowest quintile; OR),

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-carotene: OR, 0.67 [95% confidence interval (CI), –0.40–1.09];

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-carotene: OR, 0.78 (95% CI, 0.48–1.25); lycopene: OR, 0.66 (95% CI, 0.38–1.13)}. The inverse association between plasma lycopene concentrations and prostate cancer risk was limited to participants who were 65 years or older (OR, 0.47; 95% CI, 0.23–0.98) and without a family history of prostate cancer (OR, 0.48; 95% CI, 0.26–0.89). Combining, older age and a negative family history provided similar results (OR, 0.43; 95% CI, 0.18–1.02). Inverse associations between

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-carotene and prostate cancer risk were also found among younger participants (<65 years of age; OR, 0.36; 95% CI, 0.14–0.91; P_{trend} = 0.03). Combining dietary intake and plasma data confirmed our results. We found a statistically significant inverse association between higher plasma lycopene concentrations and lower risk of prostate cancer, which was restricted to older participants and those without a family history of prostate cancer. This observation suggests that tomato products may exhibit more potent protection against sporadic prostate cancer rather than those with a stronger familial or hereditary component. In addition, our findings also suggest that among younger men, diets rich in

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β -carotene, 0.55 (0.28–1.08) for lycopene and 0.37 (0.18–0.75) for total carotenoids. SNPs rs25489 in XRCC1, rs699473 in SOD3 and rs1052133 in OGG1 modified these associations for

α -carotene,

β -carotene and lycopene, respectively ($P \leq 0.05$). The proportion of men with a high degree of FGA increased with Gleason Score ($P < 0.001$). Among men with Gleason score $\leq 3 + 4$, higher lycopene levels were associated with lower FGA ($P = 0.04$). CONCLUSION: Circulating carotenoids at diagnosis, particularly among men carrying specific somatic variations, were inversely associated with risk of high-grade prostate cancer. In exploratory analyses, higher lycopene level was associated with less genomic instability among men with low-grade disease which is novel and supports the hypothesis that lycopene may inhibit progression of prostate cancer early in its natural history.", "DOI": "10.1002/pros.23125", "ISSN": "0270-4137", "author":

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β -carotene, retinol and vitamin E and prostate cancer risk", "container-title": "European Journal Of Clinical Nutrition", "page": "1235", "volume": "64", "journalAbbreviation": "European Journal Of Clinical Nutrition", "author": [{"family": "Beilby", "given": "J"}, {"family": "Ambrosini", "given": "G L"}, {"family": "Rossi", "given": "E"}, {"family": "Klerk", "given": "N H"}, {"family": "Musk", "given": "A W"}], "issued": {"date-parts": [{"2010, 8, 4}]}}, {"id": "773", "uris": ["http://zotero.org/users/2724931/items/M8ZPITDZ"], "uri": "http://zotero.org/users/2724931/items/M8ZPITDZ", "itemData": {"id": "773", "type": "article-journal", "title": "Prostate Cancer and Dietary Carotenoids", "container-title": "American Journal of Epidemiology", "page": "119-123", "volume": "151", "issue": "2", "abstract": "This population-based case-control study investigated associations between prostate cancer risk and dietary intake of the carotenoids

β -carotene and lycopene and their major plant food sources, including carrots, green leafy vegetables, and tomato-based foods. The study was carried out in Auckland, New Zealand, during 1996–1997 and recruited 317 prostate cancer cases and 480 controls. The authors found that dietary intake of

β -carotene and its main vegetable sources was largely unassociated with prostate cancer risk, whereas intake of lycopene and tomato-based foods was weakly associated with a reduced risk. These results suggest that in contrast to the findings regarding many types of cancers, vegetables rich in

β -carotene are not protective against prostate cancer. However, lycopene from tomato-based foods was found to be associated with a small reduction in risk. Am J Epidemiol 2000; 151:119–23.", "DOI": "10.1093/oxfordjournals.aje.a010176", "ISSN": "0002-9262", "journalAbbreviation": "American Journal of Epidemiology", "author": [{"family": "Norris", "given": "Alan E."}, {"family": "Jackson", "given": "Rodney T."}, {"family": "Sharpe", "given": "Susan J."}, {"family": "Skeaff", "given": "C. Murray"}], "issued": {"date-parts": [{"2000, 1, 15}]}}, {"id": "760", "uris": ["http://zotero.org/users/2724931/items/2YX9MMBA"], "uri": "http://zotero.org/users/2724931/items/2YX9MMBA", "itemData": {"id": "760", "type": "article-journal", "title": "Retinol, carotenoids and the risk of prostate cancer: A case-control study from Italy", "container-title": "International Journal of Cancer", "page": "689-692", "volume": "112", "issue": "4", "abstract": "Abstract Several studies have evaluated the possible association between intakes of retinoids and carotenoids and the risk of prostate cancer, but the evidence is still inconsistent. Further, only a few studies have investigated the role of specific carotenoids other than ?-carotene. We have thus considered the association between retinol and various carotenoids using data from a multicentric case-control study conducted in Italy between 1991 and 2002. This included 1,294 incident, histologically confirmed prostate cancer cases below age 75 years admitted to major teaching and general hospitals in the areas under study, and 1,451 controls below age 75 years selected among patients admitted to the same hospitals as cases for a wide spectrum of acute nonneoplastic conditions not related to long-term modifications of diet. Subjects' usual diet was investigated by means of a validated food-frequency questionnaire. Multivariate odds ratios and the corresponding 95% confidence intervals were estimated using unconditional logistic regression models. The risk of prostate cancer tended to decrease with increasing intake of retinol (OR = 0.79 for the highest versus the lowest quintile of intake), carotene (OR = 0.70),

α -carotene (OR = 0.85) and ?-carotene (OR = 0.72), although the estimates were significant for carotene and ?-carotene only. No meaningful associations emerged for nonprovitamin A carotenoids, such as lycopene (OR = 0.94) and lutein/zeaxanthin (OR = 0.91). No systematic heterogeneity was observed across strata of age, education and body mass index. Thus, our study supports the hypothesis of a weak protective effect of carotene, particularly ?-carotene, on the risk of prostate cancer, while it indicates that other carotenoids, including lycopene, and retinol are not appreciably related to the risk of this neoplasm. ? 2004 Wiley-Liss, Inc.", "DOI": "10.1002/ijc.20486", "ISSN": "0020-7136", "journalAbbreviation": "International Journal of Cancer", "author": [{"family": "Bosetti", "given": "Cristina"}, {"family": "Talamini", "given": "Renato"}, {"family": "Montella", "given": "Maurizio"}, {"family": "Negri", "given": "Eva"}, {"family": "Conti", "given": "Ettore"}, {"family": "Franceschi", "given": "Silvia"}, {"family": "La Vecchia", "given": "Carlo"}], "issued": {"date-parts": [{"2004, 7, 9}]}}, {"id": "770", "uris":

related genes and tumor instability. METHODS: We measured plasma levels of carotenoids and genotyped 20 single nucleotide polymorphisms (SNP) in SOD1, SOD2, SOD3, XRCC1, and OGG1 among 559 men with non-metastatic prostate cancer undergoing radical prostatectomy. We performed copy number analysis in a subset of these men (n =67) to study tumor instability assessed as Fraction of the Genome Altered (FGA). We examined associations between carotenoids, genotypes, tumor instability and risk of high-grade prostate cancer (Gleason grade $\geq 4 + 3$) using logistic and linear regression. RESULTS: Circulating carotenoid levels were inversely associated with the risk of high-grade prostate cancer; odds ratios (OR) and 95% confidence intervals (CI) comparing highest versus lowest quartiles were: 0.34 (95% CI: 0.18–0.66) for


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687","volume":"76","issue":"5","archive":"PMC","archive_location":"PMC2228001","abstract":"We interviewed
328 men diagnosed with prostate cancer before the age of 75 years and 328 age-matched population controls. The
principal hypotheses were that risk would increase with a high intake of total or saturated fat and would decrease
with a high intake of carotene (beta-carotene equivalents) or lycopene. We also examined the associations of other
nutrients and foods with risk. There was no evidence for an association between fat intake and risk, although the
average fat intake was high and the range of fat intakes was narrow (medians of lower and upper thirds of
percentage of energy from fat among controls were 34.3% and 42.9% respectively). Risk was lower in subjects
with higher carotene intake: odds ratios 0.65 (95% CI 0.45-0.94) and 0.76 (0.53-1.10) in the middle and upper
thirds of carotene intake respectively (P for trend = 0.150). Lycopene was not associated with risk. Among 13
other nutrients examined, the odds ratios in the top third of intake were below 0.8 for: potassium, 0.74 (0.51-1.09;
P for trend = 0.054); zinc, 0.73 (0.49-1.08; P for trend = 0.126); iodine, 0.75 (0.51-1.11; P for trend = 0.077);
vitamin B6 food only, 0.77 (0.53-1.12; P for trend = 0.077); and vitamin B6 including supplements, 0.70
(0.48-1.03; P for trend = 0.029). Among 18 foods examined, statistically significant associations were observed
for: garlic as food, > or = 2/week vs never, 0.56 (0.33-0.93); garlic including supplements, > or = 2/week vs never,
0.60 (0.37-0.96); baked beans, > or = 2/week vs < 1/month, 0.57 (0.34-0.95); and garden peas, > or = 5/week vs <
or = 3/month, 0.35 (0.13-0.91). This study does not support the hypothesis that fat increases risk and is equivocal
in relation to carotene. The possible relationships of vitamin B6, garlic, beans and peas with risk for prostate
cancer should be further investigated.", "ISSN": "0007-0920", "author": [{"family": "Key", "given": "T J"},
{"family": "Silcocks", "given": "P B"}, {"family": "Davey", "given": "G K"}, {"family": "Appleby", "given": "P N"},
{"family": "Bishop", "given": "D T"}], "issued": {"date-parts": [{"1997"}]}}, {"id":768,"uris":
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dietary lycopene and other carotenoids protect against prostate cancer?","container-title":"International Journal of
Cancer","page":"1010-1014","volume":"113","issue":"6","abstract":"Abstract To determine whether dietary intake
of lycopene and other carotenoids has an etiological association with prostate cancer, a case-control study was
conducted in Hangzhou, southeast China during 2001-2002. The cases were 130 incident patients with
histologically confirmed adenocarcinoma of the prostate. The controls were 274 hospital inpatients without
prostate cancer or any other malignant diseases. Information on usual food consumption, including vegetables and
fruits, was collected by face-to-face interviews using a structured food frequency questionnaire. The risks of
prostate cancer for the intake of carotenoids and selected vegetables and fruits rich in carotenoids were assessed
using multivariate logistic regression, adjusting for age, locality, education, income, body mass index, marital
status, number of children, family history of prostate cancer, tea drinking, total fat and caloric intake. The prostate
cancer risk declined with increasing consumption of lycopene,
alpha
-carotene, beta-carotene, gamma-cryptoxanthin, lutein and zeaxanthin. Intake of tomatoes, pumpkin, spinach, watermelon
and citrus fruits were also inversely associated with the prostate cancer risk. The adjusted odds ratios for the
highest versus the lowest quartiles of intake were 0.18 (95% CI: 0.08-0.41) for lycopene, 0.43 (95% CI: 0.21-
0.85) for
alpha
-carotene, 0.34 (95% CI: 0.17-0.69) for beta-carotene, 0.15 (95% CI: 0.06-0.34) for gamma-cryptoxanthin and 0.02 (95%
CI: 0.01-0.10) for lutein and zeaxanthin. The corresponding dose-response relationships were also significant,
suggesting that vegetables and fruits rich in lycopene and other carotenoids may be protective against prostate
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Study type
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Prostate Cancer","container-title":"The Prostate","page":"339-
348","volume":"76","issue":"4","archive":"PMC","archive_location":"PMC5493324","abstract":"BACKGROUND
Carotenoids are a class of nutrients with antioxidant properties that have been purported to protect against cancer.
However, the reported associations between carotenoids and prostate cancer have been heterogeneous and lacking
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data on interactions with nucleotide sequence variations and genomic biomarkers. OBJECTIVE: To examine the associations between carotenoid levels and the risk of high-grade prostate cancer, also considering antioxidant-related genes and tumor instability. METHODS: We measured plasma levels of carotenoids and genotyped 20 single nucleotide polymorphisms (SNP) in SOD1, SOD2, SOD3, XRCC1, and OGG1 among 559 men with non-metastatic prostate cancer undergoing radical prostatectomy. We performed copy number analysis in a subset of these men (n =67) to study tumor instability assessed as Fraction of the Genome Altered (FGA). We examined associations between carotenoids, genotypes, tumor instability and risk of high-grade prostate cancer (Gleason grade $\geq 4 + 3$) using logistic and linear regression. RESULTS: Circulating carotenoid levels were inversely associated with the risk of high-grade prostate cancer; odds ratios (OR) and 95% confidence intervals (CI) comparing highest versus lowest quartiles were: 0.34 (95% CI: 0.18–0.66) for

α

-carotene, 0.31 (95% CI: 0.15–0.63) for

β

-carotene, 0.55 (0.28–1.08) for lycopene and 0.37 (0.18–0.75) for total carotenoids. SNPs rs25489 in XRCC1, rs699473 in SOD3 and rs1052133 in OGG1 modified these associations for

α

-carotene,

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-carotene and lycopene, respectively ($P \leq 0.05$). The proportion of men with a high degree of FGA increased with Gleason Score ($P < 0.001$). Among men with Gleason score $\leq 3 + 4$, higher lycopene levels were associated with lower FGA ($P = 0.04$). CONCLUSION: Circulating carotenoids at diagnosis, particularly among men carrying specific somatic variations, were inversely associated with risk of high-grade prostate cancer. In exploratory analyses, higher lycopene level was associated with less genomic instability among men with low-grade disease which is novel and supports the hypothesis that lycopene may inhibit progression of prostate cancer early in its natural history.,"DOI":"10.1002/pros.23125","ISSN":"0270-4137","author":

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Case-control

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OBJECTIVE: We examine the association of antioxidants and 15-isoprostane F(2t) with risk of prostate cancer. METHODS: We conducted a nested case–control study of serum antioxidant biomarkers (selenium, tocopherols, carotenoids, and retinol) and a urinary oxidation biomarker (15-isoprostane F(2t)) with risk of prostate cancer within the Multiethnic Cohort. Demographic, dietary, and other exposure information was collected by self-administered questionnaire in 1993–1996. We compared prediagnostic biomarker levels from 467 prostate cancer cases and 936 cancer free controls that were matched on several variables. Multivariate conditional logistic regression models were used to compute adjusted odds ratios (ORs) and 95% confidence intervals (CIs). RESULTS: We observed that there was no overall association of serum concentrations of antioxidants and urinary concentrations of 15-isoprostane F(2t) with risk of prostate cancer or risk of advanced prostate cancer. However, we did observe an inverse association for serum selenium only among African-American men (p trend = 0.02); men in the third tertile of selenium concentrations had a 41% lower risk (95% CI: 0.38–0.93) of prostate cancer when compared to men in the first tertile. CONCLUSIONS: Overall, our study found no association of serum antioxidants or 15-isoprostane F(2t) with the risk of prostate cancer. The observed inverse association of selenium with prostate cancer in African-Americans needs to be validated in other studies.,"DOI":"10.1007/s10552-009-9304-4","ISSN":"0957-5243","author":[{"family":"Gill","given":"Jasmeet K"}, {"family":"Franke","given":"Adrian A"}, {"family":"Morris","given":"J Steven"}, {"family":"Cooney","given":"Robert V"}, {"family":"Wilkens","given":"Lynne R"}, {"family":"Le Marchand","given":"Loic"}, {"family":"Goodman","given":"Marc T"}, {"family":"Henderson","given":"Brian E"}, {"family":"Kolonel","given":"Laurence N"}], "issued":{"date-parts":["2009",9]} }}, {"id":"767","uris":["http://zotero.org/users/2724931/items/G2VXZNAR"],"uri":["http://zotero.org/users/2724931/items/G2VXZNAR"],"itemData":{"id":"767","type":"article-journal","title":"The Association between Lung and Prostate Cancer Risk, and Serum Micronutrients","container-title":"Cancer Epidemiology Biomarkers & Prevention","page":"518","volume":"12","issue":"6","abstract":"

β

-Carotene and Retinol Efficacy Trial is a nationwide chemoprevention trial that recruited 18,314 high-risk individuals to test the effect of supplemental

β

-carotene and retinol on lung cancer incidence. In this report, we conducted a prospective nested case-control study of the association between serum carotenoids, retinoids, and tocopherols on both lung and prostate cancer incidence. Prerandomization serum samples were selected from 278 lung cancer cases and 205 prostate cancer cases, and 483 controls matched by high-risk population, study center location, age, sex (lung cancer only), smoking status, and year of randomization. Carotenoids, retinoids, and tocopherols were analyzed by high-

performance liquid chromatography. Endpoints were confirmed by pathology review (lung cancer) or review of the pathology report (prostate cancer). In the control-only population, there was a significant association between tobacco use and serum micronutrient concentration. Current smokers compared with former smokers had lower mean levels of all of the micronutrients tested with zeaxanthin,

β

-cryptoxanthin,

α

-carotene,

α

-tocopherol, retinol, and retinyl palmitate reaching statistical significance at $P = 0.05$. In the overall population, the mean serum concentrations of all of the micronutrients except

γ

-tocopherol were lower for lung cancer cases than controls. Statistically significant trends across quartiles were observed in lutein ($P = 0.02$), zeaxanthin ($P = 0.02$), and

α

-tocopherol ($P = 0.03$). The carotenoid findings in the overall population were because of the strong inverse association between serum micronutrients and lung cancer in females. Statistically significant odds ratios (ORs) comparing 4th to 1st quartiles in the female population were seen in lutein [OR, 0.31; confidence interval (CI), 0.13–0.75], zeaxanthin (OR, 0.31; CI, 0.12–0.77), and

β

-cryptoxanthin (OR, 0.34; CI, 0.14–0.81). For prostate cancer, mean serum concentrations were lower in cases for all of the nutrients except

α

-carotene. Only for

α

-tocopherol (Ptrend = 0.04) were the findings statistically significant. There was no statistically significant association between serum carotenoids and prostate cancer. Our findings provide additional support for the association between physiological levels of dietary micronutrients and cancer

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the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial", "container-title": "Cancer Epidemiology

Biomarkers & Prevention", "page": "962", "volume": "16", "issue": "5", "abstract": "Background: Reports from

several studies have suggested that carotenoids, and in particular lycopene, could be prostate cancer-preventive

agents. This has stimulated extensive laboratory and clinical research, as well as much commercial and public

enthusiasm. However, the epidemiologic evidence remains inconclusive. Materials and Methods: We investigated

the association between prediagnostic serum carotenoids (lycopene,

α

-carotene,

β

-carotene,

β

-cryptoxanthin, lutein, and zeaxanthin) and risk of prostate cancer in the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial, a multicenter study designed to examine methods of early detection and risk factors for cancer. The study included 692 incident prostate cancer cases, diagnosed 1 to 8 years after study entry, including 270 aggressive cases, with regional or distant stage ($n = 90$) or Gleason score ≥ 7 ($n = 235$), and 844 randomly selected, matched controls. As study participants were selected from those who were assigned to annual standardized screening for prostate cancer, results are unlikely to be biased by differential screening, a circumstance that is difficult to attain under non-trial conditions. Results: No association was observed between serum lycopene and total prostate cancer [odds ratios (OR), 1.14; 95% confidence intervals (95% CI), 0.82–1.58 for highest versus lowest quintile; P for trend, 0.28] or aggressive prostate cancer (OR, 0.99; 95% CI, 0.62–1.57 for highest versus lowest quintile; P for trend, 0.433).

β

-Carotene was associated with an increased risk of aggressive prostate cancer (OR, 1.67; 95% CI, 1.03–2.72 for highest versus lowest quintile; P for trend, 0.13); in particular, regional or distant stage disease (OR, 3.16; 95% CI, 1.37–7.31 for highest versus lowest quintile; P for trend, 0.02); other carotenoids were not associated with risk.

Conclusion: In this large prospective study, high serum

β

-carotene concentrations were associated with increased risk for aggressive, clinically relevant prostate cancer.

Lycopene and other carotenoids were unrelated to prostate cancer. Consistent with other recent publications, these results suggest that lycopene or tomato-based regimens will not be effective for prostate cancer prevention.

(Cancer Epidemiol Biomarkers Prev 2007;16(5):962–8)", "DOI": "10.1158/1055-9965.EPI-06-

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Epidemiology Biomarkers & Prevention", "page": "260", "volume": "13", "issue": "2", "abstract": "The

association between plasma carotenoids and prostate cancer risk was investigated in a case-control study nested

within the prospective Health Professionals Follow-up Study. We matched 450 incident prostate cancer cases

diagnosed from 1993–1998 to 450 controls by age, time, month, and year of blood donation. Modest inverse, but

not statistically significant, associations were observed among plasma

α

-carotene,

β
 -carotene, and lycopene concentrations, and overall risk of prostate cancer diagnosis {odds ratio (highest versus lowest quintile; OR),
 α
 -carotene: OR, 0.67 [95% confidence interval (CI), -0.40–1.09];
 β
 -carotene: OR, 0.78 (95% CI, 0.48–1.25); lycopene: OR, 0.66 (95% CI, 0.38–1.13)}. The inverse association between plasma lycopene concentrations and prostate cancer risk was limited to participants who were 65 years or older (OR, 0.47; 95% CI, 0.23–0.98) and without a family history of prostate cancer (OR, 0.48; 95% CI, 0.26–0.89). Combining, older age and a negative family history provided similar results (OR, 0.43; 95% CI, 0.18–1.02). Inverse associations between
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 -carotene and prostate cancer risk were also found among younger participants (<65 years of age; OR, 0.36; 95% CI, 0.14–0.91; P_{trend} = 0.03). Combining dietary intake and plasma data confirmed our results. We found a statistically significant inverse association between higher plasma lycopene concentrations and lower risk of prostate cancer, which was restricted to older participants and those without a family history of prostate cancer. This observation suggests that tomato products may exhibit more potent protection against sporadic prostate cancer rather than those with a stronger familial or hereditary component. In addition, our findings also suggest that among younger men, diets rich in
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 -carotene may also play a protective role in prostate carcinogenesis." "DOI": "10.1158/1055-9965.EPI-03-0012", "journalAbbreviation": "Cancer Epidemiol Biomarkers Prev", "author": [{"family": "Wu", "given": "Kana"}, {"family": "Erdman", "given": "John W."}, {"family": "Schwartz", "given": "Steven J."}, {"family": "Platz", "given": "Elizabeth A."}, {"family": "Leitzmann", "given": "Michael"}, {"family": "Clinton", "given": "Steven K."}, {"family": "DeGroot", "given": "Valerie"}, {"family": "Willett", "given": "Walter C."}, {"family": "Giovannucci", "given": "Edward"}], "issued": {"date-parts": [{"2004", "2", "1"}]}, {"id": "771", "uris": [{"http://zotero.org/users/2724931/items/XXKA5QES"}], "uri": [{"http://zotero.org/users/2724931/items/XXKA5QES"}], "itemData": {"id": "771", "type": "article-journal", "title": "A Prospective Study of Lycopene and Tomato Product Intake and Risk of Prostate Cancer", "container-title": "Cancer Epidemiology Biomarkers & Prevention", "page": "92", "volume": "15", "issue": "1", "abstract": "Background: Dietary lycopene and tomato products may reduce risk of prostate cancer; however, uncertainty remains about this possible association. Methods: We evaluated the association between intake of lycopene and specific tomato products and prostate cancer risk in the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial, a multicenter study designed to investigate cancer early detection methods and etiologic determinants. Participants completed both a general risk factor and a 137-item food frequency questionnaire at baseline. A total of 1,338 cases of prostate cancer were identified among 29,361 men during an average of 4.2 years of follow-up. Results: Lycopene intake was not associated with prostate cancer risk. Reduced risks were also not found for total tomato servings or for most tomato-based foods. Statistically nonsignificant inverse associations were noted for pizza [all prostate cancer: relative risk (RR), 0.83; 95% confidence interval (95% CI), 0.67–1.03 for ≥ 1 serving/wk versus <0.5 serving/mo; P_{trend} = 0.06 and advanced prostate cancer: RR, 0.79; 95% CI, 0.56–1.10; P_{trend} = 0.12] and spaghetti/tomato sauce consumption (advanced prostate cancer: RR = 0.81, 95% CI, 0.57–1.16 for ≥ 2 servings/wk versus <1 serving/mo; P_{trend} = 0.31). Among men with a family history of prostate cancer, risks were decreased in relation to increased consumption of lycopene (P_{trend} = 0.04) and specific tomato-based foods commonly eaten with fat (spaghetti, P_{trend} = 0.12; pizza, P_{trend} = 0.15; lasagna, P_{trend} = 0.02). Conclusions: This large study does not support the hypothesis that greater lycopene/tomato product consumption protects from prostate cancer. Evidence for protective associations in subjects with a family history of prostate cancer requires further corroboration. (Cancer Epidemiol Biomarkers Prev 2006;15(1):92–8)", "DOI": "10.1158/1055-9965.EPI-05-0563", "journalAbbreviation": "Cancer Epidemiol Biomarkers Prev", "author": [{"family": "Kirsh", "given": "Victoria A."}, {"family": "Mayne", "given": "Susan T."}, {"family": "Peters", "given": "Ulrike"}, {"family": "Chatterjee", "given": "Nilanjan"}, {"family": "Leitzmann", "given": "Michael F."}, {"family": "Dixon", "given": "L. Beth"}, {"family": "Urban", "given": "Donald A."}, {"family": "Crawford", "given": "E. David"}, {"family": "Hayes", "given": "Richard B."}], "issued": {"date-parts": [{"2006", "1", "1"}]}, {"id": "759", "uris": [{"http://zotero.org/users/2724931/items/UC8EM9WV"}], "uri": [{"http://zotero.org/users/2724931/items/UC8EM9WV"}], "itemData": {"id": "759", "type": "article-journal", "title": "Serum levels of folate, lycopene,
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 -carotene and lycopene and their major plant food sources, including carrots, green leafy vegetables, and tomato-based foods. The study was carried out in Auckland, New Zealand, during 1996–1997 and recruited 317 prostate cancer cases and 480 controls. The authors found that dietary intake of
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 -carotene and its main vegetable sources was largely unassociated with prostate cancer risk, whereas intake of lycopene and tomato-based foods was weakly associated with a reduced risk. These results suggest that in contrast to the findings regarding many types of cancers, vegetables rich in
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 -carotene are not protective against prostate cancer. However, lycopene from tomato-based foods was found to be associated with a small reduction in risk. Am J Epidemiol 2000; 151:119–23.", "DOI": "10.1093/oxfordjournals.aje.a010176", "ISSN": "0002-9262", "journalAbbreviation": "American Journal of Epidemiology", "author": [{"family": "Norris", "given": "Alan E."}, {"family": "Jackson", "given": "Rodney T."}, {"family": "Sharpe", "given": "Susan J."}, {"family": "Skeaff", "given": "C. Murray"}], "issued": {"date-parts": [{"2000", "1", "15"}]}, {"id": "760", "uris": [{"http://zotero.org/users/2724931/items/2YX9MMA"}], "uri":

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-carotene (OR = 0.85) and β -carotene (OR = 0.72), although the estimates were significant for carotene and β -carotene only. No meaningful associations emerged for nonprovitamin A carotenoids, such as lycopene (OR = 0.94) and lutein/zeaxanthin (OR = 0.91). No systematic heterogeneity was observed across strata of age, education and body mass index. Thus, our study supports the hypothesis of a weak protective effect of carotene, particularly β -carotene, on the risk of prostate cancer, while it indicates that other carotenoids, including lycopene, and retinol are not appreciably related to the risk of this neoplasm. © 2004 Wiley-Liss, Inc., "DOI": "10.1002/ijc.20486", "ISSN": "0020-7136", "journalAbbreviation": "International Journal of Cancer", "author": [{"family": "Bosetti", "given": "Cristina"}, {"family": "Talamini", "given": "Renato"}, {"family": "Montella", "given": "Maurizio"}, {"family": "Negri", "given": "Eva"}, {"family": "Conti", "given": "Ettore"}, {"family": "Franceschi", "given": "Silvia"}, {"family": "La Vecchia", "given": "Carlo"}], "issued": {"date-parts": [{"2004", "7", "9"}]}, {"id": "770", "uris":

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-carotene, β -carotene, β -cryptoxanthin, lutein and zeaxanthin. Intake of tomatoes, pumpkin, spinach, watermelon and citrus fruits were also inversely associated with the prostate cancer risk. The adjusted odds ratios for the highest versus the lowest quartiles of intake were 0.18 (95% CI: 0.08-0.41) for lycopene, 0.43 (95% CI: 0.21-0.85) for

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-carotene, 0.34 (95% CI: 0.17-0.69) for β -carotene, 0.15 (95% CI: 0.06-0.34) for β -cryptoxanthin and 0.02 (95% CI: 0.01-0.10) for lutein and zeaxanthin. The corresponding dose-response relationships were also significant, suggesting that vegetables and fruits rich in lycopene and other carotenoids may be protective against prostate cancer. © 2004 Wiley-Liss, Inc., "DOI": "10.1002/ijc.20667", "ISSN": "0020-7136", "journalAbbreviation": "International Journal of Cancer", "author": [{"family": "Jian", "given": "Le"}, {"family": "Du", "given": "Chuan-Jun"}, {"family": "Lee", "given": "Andy H."}, {"family": "Binns", "given": "Colin W."}], "issued": {"date-parts": [{"2004", "10", "28"}]}, {"schema": "https://github.com/citation-style-language/schema/raw/master/csl-citation.json"}]

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    studies have evaluated the possible association between intakes of retinoids and carotenoids and the risk of
    prostate cancer, but the evidence is still inconsistent. Further, only a few studies have investigated the role of
    specific carotenoids other than ?-carotene. We have thus considered the association between retinol and various
    carotenoids using data from a multicentric case-control study conducted in Italy between 1991 and 2002. This
    included 1,294 incident, histologically confirmed prostate cancer cases below age 75 years admitted to major
    teaching and general hospitals in the areas under study, and 1,451 controls below age 75 years selected among
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    to long-term modifications of diet. Subjects' usual diet was investigated by means of a validated food-frequency
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    -carotene (OR = 0.85) and ?-carotene (OR = 0.72), although the estimates were significant for carotene and ?
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    and body mass index. Thus, our study supports the hypothesis of a weak protective effect of carotene,
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-Carotene and Retinol Efficacy Trial is a nationwide chemoprevention trial that recruited 18,314 high-risk individuals to test the effect of supplemental

cases, and 483 controls matched by high-risk population, study center location, age, sex (lung cancer only), smoking status, and year of randomization. Carotenoids, retinoids, and tocopherols were analyzed by high-performance liquid chromatography. Endpoints were confirmed by pathology review (lung cancer) or review of the pathology report (prostate cancer). In the control-only population, there was a significant association between tobacco use and serum micronutrient concentration. Current smokers compared with former smokers had lower mean levels of all of the micronutrients tested with zeaxanthin,

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-cryptoxanthin,

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-carotene,

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-tocopherol, retinol, and retinyl palmitate reaching statistical significance at $P = 0.05$. In the overall population, the mean serum concentrations of all of the micronutrients except

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-tocopherol were lower for lung cancer cases than controls. Statistically significant trends across quartiles were observed in lutein ($P = 0.02$), zeaxanthin ($P = 0.02$), and

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-tocopherol ($P = 0.03$). The carotenoid findings in the overall population were because of the strong inverse association between serum micronutrients and lung cancer in females. Statistically significant odds ratios (ORs) comparing 4th to 1st quartiles in the female population were seen in lutein [OR, 0.31; confidence interval (CI), 0.13–0.75], zeaxanthin (OR, 0.31; CI, 0.12–0.77), and

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-cryptoxanthin (OR, 0.34; CI, 0.14–0.81). For prostate cancer, mean serum concentrations were lower in cases for all of the nutrients except

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-carotene. Only for

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-tocopherol ($P_{trend} = 0.04$) were the findings statistically significant. There was no statistically significant association between serum carotenoids and prostate cancer. Our findings provide additional support for the association between physiological levels of dietary micronutrients and cancer incidence.", "journalAbbreviation": "Cancer Epidemiol Biomarkers Prev", "author": [{"family": "Goodman", "given": "Gary E."}, {"family": "Schaffer", "given": "Steven"}, {"family": "Omenn", "given": "Gilbert S."}, {"family": "Chen", "given": "Chu"}, {"family": "King", "given": "Irena"}], "issued": {"date-parts": ["2003", 6, 1]}}, {"id": 775, "uris": ["http://zotero.org/users/2724931/items/6GDCVHDT"], "uri": ["http://zotero.org/users/2724931/items/6GDCVHDT"], "itemData": {"id": 775, "type": "article-journal", "title": "Serum Lycopene, Other Carotenoids, and Prostate Cancer Risk: a Nested Case-Control Study in the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial", "container-title": "Cancer Epidemiology Biomarkers & Prevention", "page": "962", "volume": "16", "issue": "5", "abstract": "Background: Reports from several studies have suggested that carotenoids, and in particular lycopene, could be prostate cancer-preventive agents. This has stimulated extensive laboratory and clinical research, as well as much commercial and public enthusiasm. However, the epidemiologic evidence remains inconclusive. Materials and Methods: We investigated the association between prediagnostic serum carotenoids (lycopene,

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-cryptoxanthin, lutein, and zeaxanthin) and risk of prostate cancer in the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial, a multicenter study designed to examine methods of early detection and risk factors for cancer. The study included 692 incident prostate cancer cases, diagnosed 1 to 8 years after study entry, including 270 aggressive cases, with regional or distant stage ($n = 90$) or Gleason score ≥ 7 ($n = 235$), and 844 randomly selected, matched controls. As study participants were selected from those who were assigned to annual standardized screening for prostate cancer, results are unlikely to be biased by differential screening, a circumstance that is difficult to attain under non-trial conditions. Results: No association was observed between serum lycopene and total prostate cancer [odds ratios (OR), 1.14; 95% confidence intervals (95% CI), 0.82–1.58 for highest versus lowest quintile; P for trend, 0.28] or aggressive prostate cancer (OR, 0.99; 95% CI, 0.62–1.57 for highest versus lowest quintile; P for trend, 0.433).

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-Carotene was associated with an increased risk of aggressive prostate cancer (OR, 1.67; 95% CI, 1.03–2.72 for highest versus lowest quintile; P for trend, 0.13); in particular, regional or distant stage disease (OR, 3.16; 95% CI, 1.37–7.31 for highest versus lowest quintile; P for trend, 0.02); other carotenoids were not associated with risk. Conclusion: In this large prospective study, high serum

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-carotene concentrations were associated with increased risk for aggressive, clinically relevant prostate cancer. Lycopene and other carotenoids were unrelated to prostate cancer. Consistent with other recent publications, these results suggest that lycopene or tomato-based regimens will not be effective for prostate cancer prevention. (Cancer Epidemiol Biomarkers Prev 2007;16(5):962–8)", "DOI": "10.1158/1055-9965.EPI-06-0861", "journalAbbreviation": "Cancer Epidemiol Biomarkers Prev", "author": [{"family": "Peters", "given": "Ulrike"}, {"family": "Leitzmann", "given": "Michael F."}, {"family": "Chatterjee", "given": "Nilanjan"}, {"family": "Wang", "given": "Yinghui"}, {"family": "Albanes", "given": "Demetrios"}, {"family": "Germann", "given": "Edward P."}, {"family": "Friesen", "given": "Marlin D."}, {"family": "Riboli", "given": "Elio"}, {"family": "Hayes", "given": "Richard B."}], "issued": {"date-parts": ["2007", 5, 1]}}, {"id": 776, "uris": ["http://zotero.org/users/2724931/items/QIHKN2VR"], "uri": ["http://zotero.org/users/2724931/items/QIHKN2VR"], "itemData": {"id": 776, "type": "article-journal", "title": "Plasma and Dietary Carotenoids, and the Risk of Prostate Cancer", "container-title": "Cancer Epidemiology Biomarkers & Prevention", "page": "260", "volume": "13", "issue": "2", "abstract": "The association between plasma carotenoids and prostate cancer risk was investigated in a case-control study nested within the prospective Health Professionals Follow-up Study. We matched 450 incident prostate cancer cases diagnosed from 1993–1998 to 450 controls by age, time, month, and year of blood donation. Modest inverse, but not statistically significant, associations were observed among plasma

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-carotene, and lycopene concentrations, and overall risk of prostate cancer diagnosis {odds ratio (highest versus lowest quintile; OR),

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-carotene: OR, 0.67 [95% confidence interval (CI), -0.40–1.09];

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-carotene: OR, 0.78 (95% CI, 0.48–1.25); lycopene: OR, 0.66 (95% CI, 0.38–1.13)}. The inverse association between plasma lycopene concentrations and prostate cancer risk was limited to participants who were 65 years or older (OR, 0.47; 95% CI, 0.23–0.98) and without a family history of prostate cancer (OR, 0.48; 95% CI, 0.26–0.89). Combining, older age and a negative family history provided similar results (OR, 0.43; 95% CI, 0.18–1.02). Inverse associations between

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-carotene and prostate cancer risk were also found among younger participants (<65 years of age; OR, 0.36; 95% CI, 0.14–0.91; P_{trend} = 0.03). Combining dietary intake and plasma data confirmed our results. We found a statistically significant inverse association between higher plasma lycopene concentrations and lower risk of prostate cancer, which was restricted to older participants and those without a family history of prostate cancer. This observation suggests that tomato products may exhibit more potent protection against sporadic prostate cancer rather than those with a stronger familial or hereditary component. In addition, our findings also suggest that among younger men, diets rich in

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-carotene may also play a protective role in prostate carcinogenesis.","DOI":"10.1158/1055-9965.EPI-03-0012","journalAbbreviation":"Cancer Epidemiol Biomarkers Prev","author":{"family":"Wu","given":"Kana"}, {"family":"Erdman","given":"John W."}, {"family":"Schwartz","given":"Steven J."}, {"family":"Platz","given":"Elizabeth A."}, {"family":"Leitzmann","given":"Michael"}, {"family":"Clinton","given":"Steven K."}, {"family":"DeGroot","given":"Valerie"}, {"family":"Willett","given":"Walter C."}, {"family":"Giovannucci","given":"Edward"}], "issued":{"date-parts": [{"2004", 2, 1}]}}, {"id": 771, "uris": [{"http://zotero.org/users/2724931/items/XXKA5QES"}], "uri": [{"http://zotero.org/users/2724931/items/XXKA5QES"}], "itemData": {"id": 771, "type": "article-journal", "title": "A Prospective Study of Lycopene and Tomato Product Intake and Risk of Prostate Cancer", "container-title": "Cancer Epidemiology Biomarkers & Prevention", "page": "92", "volume": "15", "issue": "1", "abstract": "Background: Dietary lycopene and tomato products may reduce risk of prostate cancer; however, uncertainty remains about this possible association. Methods: We evaluated the association between intake of lycopene and specific tomato products and prostate cancer risk in the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial, a multicenter study designed to investigate cancer early detection methods and etiologic determinants. Participants completed both a general risk factor and a 137-item food frequency questionnaire at baseline. A total of 1,338 cases of prostate cancer were identified among 29,361 men during an average of 4.2 years of follow-up. Results: Lycopene intake was not associated with prostate cancer risk. Reduced risks were also not found for total tomato servings or for most tomato-based foods. Statistically nonsignificant inverse associations were noted for pizza [all prostate cancer: relative risk (RR), 0.83; 95% confidence interval (95% CI), 0.67-1.03 for ≥ 1 serving/wk versus < 0.5 serving/mo; P_{trend} = 0.06 and advanced prostate cancer: RR, 0.79; 95% CI, 0.56-1.10; P_{trend} = 0.12] and spaghetti/tomato sauce consumption (advanced prostate cancer: RR = 0.81, 95% CI, 0.57-1.16 for ≥ 2 servings/wk versus < 1 serving/mo; P_{trend} = 0.31). Among men with a family history of prostate cancer, risks were decreased in relation to increased consumption of lycopene (P_{trend} = 0.04) and specific tomato-based foods commonly eaten with fat (spaghetti, P_{trend} = 0.12; pizza, P_{trend} = 0.15; lasagna, P_{trend} = 0.02). Conclusions: This large study does not support the hypothesis that greater lycopene/tomato product consumption protects from prostate cancer. Evidence for protective associations in subjects with a family history of prostate cancer requires further corroboration. (Cancer Epidemiol Biomarkers Prev 2006;15(1):92-8)", "DOI":"10.1158/1055-9965.EPI-05-0563", "journalAbbreviation":"Cancer Epidemiol Biomarkers Prev", "author": [{"family":"Kirsh","given":"Victoria A."}, {"family":"Mayne","given":"Susan T."}, {"family":"Peters","given":"Ulrike"}, {"family":"Chatterjee","given":"Nilanjan"}, {"family":"Leitzmann","given":"Michael F."}, {"family":"Dixon","given":"L. Beth"}, {"family":"Urban","given":"Donald A."}, {"family":"Crawford","given":"E. David"}, {"family":"Hayes","given":"Richard B."}], "issued":{"date-parts": [{"2006", 1, 1}]}}, {"id": 772, "uris": [{"http://zotero.org/users/2724931/items/Z88XYJCK"}], "uri": [{"http://zotero.org/users/2724931/items/Z88XYJCK"}], "itemData": {"id": 772, "type": "article-journal", "title": "Associations Between Circulating Carotenoids, Genomic Instability and the Risk of High-Grade Prostate Cancer", "container-title": "The Prostate", "page": "339-348", "volume": "76", "issue": "4", "archive": "PMC", "archive_location": "PMC5493324", "abstract": "BACKGROUND: Carotenoids are a class of nutrients with antioxidant properties that have been purported to protect against cancer. However, the reported associations between carotenoids and prostate cancer have been heterogeneous and lacking data on interactions with nucleotide sequence variations and genomic biomarkers. OBJECTIVE: To examine the associations between carotenoid levels and the risk of high-grade prostate cancer, also considering antioxidant-related genes and tumor instability. METHODS: We measured plasma levels of carotenoids and genotyped 20 single nucleotide polymorphisms (SNP) in SOD1, SOD2, SOD3, XRCC1, and OGG1 among 559 men with non-metastatic prostate cancer undergoing radical prostatectomy. We performed copy number analysis in a subset of these men (n = 67) to study tumor instability assessed as Fraction of the Genome Altered (FGA). We examined associations between carotenoids, genotypes, tumor instability and risk of high-grade prostate cancer (Gleason grade $\geq 4 + 3$) using logistic and linear regression. RESULTS: Circulating carotenoid levels were inversely associated with the risk of high-grade prostate cancer; odds ratios (OR) and 95% confidence intervals (CI) comparing highest versus lowest quartiles were: 0.34 (95% CI: 0.18–0.66) for

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-carotene, 0.55 (0.28–1.08) for lycopene and 0.37 (0.18–0.75) for total carotenoids. SNPs rs25489 in XRCC1, rs699473 in SOD3 and rs1052133 in OGG1 modified these associations for

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-carotene and lycopene, respectively (P ≤ 0.05). The proportion of men with a high degree of FGA increased with Gleason Score (P < 0.001). Among men with Gleason score $\leq 3 + 4$, higher lycopene levels were associated with

lower FGA ($P = 0.04$). CONCLUSION: Circulating carotenoids at diagnosis, particularly among men carrying specific somatic variations, were inversely associated with risk of high-grade prostate cancer. In exploratory analyses, higher lycopene level was associated with less genomic instability among men with low-grade disease which is novel and supports the hypothesis that lycopene may inhibit progression of prostate cancer early in its natural history.", "DOI": "10.1002/pros.23125", "ISSN": "0270-4137", "author":

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-carotene, retinol and vitamin E and prostate cancer risk", "container-title": "European Journal Of Clinical Nutrition", "page": "1235", "volume": "64", "journalAbbreviation": "European Journal Of Clinical Nutrition", "author": [{"family": "Beilby", "given": "J"}, {"family": "Ambrosini", "given": "G L"}, {"family": "Rossi", "given": "E"}, {"family": "Klerk", "given": "N H", "non-dropping-particle": "de"}, {"family": "Musk", "given": "A W"}], "issued": {"date-parts": [{"2010", 8, 4}]}}], {"id": 773, "uris": ["http://zotero.org/users/2724931/items/M8ZPITDZ"], "uri":

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-carotene and lycopene and their major plant food sources, including carrots, green leafy vegetables, and tomato-based foods. The study was carried out in Auckland, New Zealand, during 1996–1997 and recruited 317 prostate cancer cases and 480 controls. The authors found that dietary intake of

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-carotene and its main vegetable sources was largely unassociated with prostate cancer risk, whereas intake of lycopene and tomato-based foods was weakly associated with a reduced risk. These results suggest that in contrast to the findings regarding many types of cancers, vegetables rich in

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-carotene are not protective against prostate cancer. However, lycopene from tomato-based foods was found to be associated with a small reduction in risk. Am J Epidemiol 2000; 151:119-23.", "DOI": "10.1093/oxfordjournals.aje.a010176", "ISSN": "0002-9262", "journalAbbreviation": "American Journal of Epidemiology", "author": [{"family": "Norris", "given": "Alan E."}, {"family": "Jackson", "given": "Rodney T."}, {"family": "Sharpe", "given": "Susan J."}, {"family": "Skeaff", "given": "C. Murray"}], "issued": {"date-parts": [{"2000", 1, 15}]}}], "schema": "https://github.com/citation-style-language/schema/raw/master/csl-citation.json"}]

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We compared prediagnostic biomarker levels from 467 prostate cancer cases and 936 cancer free controls that were matched on several variables. Multivariate conditional logistic regression models were used to compute adjusted odds ratios (ORs) and 95% confidence intervals (CIs). RESULTS: We observed that there was no overall association of serum concentrations of antioxidants and urinary concentrations of 15-isoprostane F(2t) with risk of prostate cancer or risk of advanced prostate cancer. However, we did observe an inverse association for serum selenium only among African-American men (p trend = 0.02); men in the third tertile of selenium concentrations had a 41% lower risk (95% CI: 0.38-0.93) of prostate cancer when compared to men in the first tertile. CONCLUSIONS: Overall, our study found no association of serum antioxidants or 15-isoprostane F(2t) with the risk of prostate cancer. The observed inverse association of selenium with prostate cancer in African-Americans needs to be validated in other studies."},"DOI":"10.1007/s10552-009-9304-4","ISSN":"0957-5243","author":[{"family":"Gill","given":"Jasmeet K"}, {"family":"Franke","given":"Adrian A"}, {"family":"Morris","given":"J Steven"}, {"family":"Cooney","given":"Robert V"}, {"family":"Wilkens","given":"Lynne R"}, {"family":"Le Marchand","given":"Loic"}, {"family":"Goodman","given":"Marc T"}, {"family":"Henderson","given":"Brian E"}, {"family":"Kolonel","given":"Laurence N"}],"issued":{"date-parts":["2009",9]}},{id":767,"uris":["http://zotero.org/users/2724931/items/G2VXZNR"],"uri":["http://zotero.org/users/2724931/items/G2VXZNR"],"itemData":{"id":767,"type":"article-journal","title":"The Association between Lung and Prostate Cancer Risk, and Serum Micronutrients","container-title":"Cancer Epidemiology Biomarkers & Prevention","page":"518","volume":"12","issue":"6","abstract":" β -Carotene and Retinol Efficacy Trial is a nationwide chemoprevention trial that recruited 18,314 high-risk individuals to test the effect of supplemental β -carotene and retinol on lung cancer incidence. In this report, we conducted a prospective nested case-control study of the association between serum carotenoids, retinoids, and tocopherols on both lung and prostate cancer incidence. Prerandomization serum samples were selected from 278 lung cancer cases and 205 prostate cancer cases, and 483 controls matched by high-risk population, study center location, age, sex (lung cancer only), smoking status, and year of randomization. Carotenoids, retinoids, and tocopherols were analyzed by high-performance liquid chromatography. Endpoints were confirmed by pathology review (lung cancer) or review of the pathology report (prostate cancer). In the control-only population, there was a significant association between tobacco use and serum micronutrient concentration. Current smokers compared with former smokers had lower mean levels of all of the micronutrients tested with zeaxanthin, β -cryptoxanthin, α -carotene, α -tocopherol, retinol, and retinyl palmitate reaching statistical significance at $P = 0.05$. In the overall population, the mean serum concentrations of all of the micronutrients except γ -tocopherol were lower for lung cancer cases than controls. Statistically significant trends across quartiles were observed in lutein ($P = 0.02$), zeaxanthin ($P = 0.02$), and α -tocopherol ($P = 0.03$). The carotenoid findings in the overall population were because of the strong inverse association between serum micronutrients and lung cancer in females. Statistically significant odds ratios (ORs) comparing 4th to 1st quartiles in the female population were seen in lutein [OR, 0.31; confidence interval (CI), 0.13-0.75], zeaxanthin (OR, 0.31; CI, 0.12-0.77), and β -cryptoxanthin (OR, 0.34; CI, 0.14-0.81). For prostate cancer, mean serum concentrations were lower in cases for all of the nutrients except α -carotene. Only for α -tocopherol (Ptrend = 0.04) were the findings statistically significant. There was no statistically significant association between serum carotenoids and prostate cancer. Our findings provide additional support for the association between physiological levels of dietary micronutrients and cancer incidence."},"journalAbbreviation":"Cancer Epidemiol Biomarkers Prev","author":[{"family":"Goodman","given":"Gary E."}, {"family":"Schaffer","given":"Steven"}, {"family":"Omenn","given":"Gilbert S."}, {"family":"Chen","given":"Chu"}, {"family":"King","given":"Irena"}],"issued":{"date-parts":["2003",6,1]}},{id":775,"uris":["http://zotero.org/users/2724931/items/6GDCVHDT"],"uri":["http://zotero.org/users/2724931/items/6GDCVHDT"],"itemData":{"id":775,"type":"article-journal","title":"Serum Lycopene, Other Carotenoids, and Prostate Cancer Risk: a Nested Case-Control Study in the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial","container-title":"Cancer Epidemiology Biomarkers & Prevention","page":"962","volume":"16","issue":"5","abstract":"Background: Reports from several studies have suggested that carotenoids, and in particular lycopene, could be prostate cancer-preventive agents. This has stimulated extensive laboratory and clinical research, as well as much commercial and public enthusiasm. However, the epidemiologic evidence remains inconclusive. Materials and Methods: We investigated the association between prediagnostic serum carotenoids (lycopene,

-carotene,

β

-cryptoxanthin, lutein, and zeaxanthin) and risk of prostate cancer in the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial, a multicenter study designed to examine methods of early detection and risk factors for cancer. The study included 692 incident prostate cancer cases, diagnosed 1 to 8 years after study entry, including 270 aggressive cases, with regional or distant stage (n = 90) or Gleason score ≥ 7 (n = 235), and 844 randomly selected, matched controls. As study participants were selected from those who were assigned to annual standardized screening for prostate cancer, results are unlikely to be biased by differential screening, a circumstance that is difficult to attain under non-trial conditions. Results: No association was observed between serum lycopene and total prostate cancer [odds ratios (OR), 1.14; 95% confidence intervals (95% CI), 0.82-1.58 for highest versus lowest quintile; P for trend, 0.28] or aggressive prostate cancer (OR, 0.99; 95% CI, 0.62-1.57 for highest versus lowest quintile; P for trend, 0.433).

β

-Carotene was associated with an increased risk of aggressive prostate cancer (OR, 1.67; 95% CI, 1.03-2.72 for highest versus lowest quintile; P for trend, 0.13); in particular, regional or distant stage disease (OR, 3.16; 95% CI, 1.37-7.31 for highest versus lowest quintile; P for trend, 0.02); other carotenoids were not associated with risk. Conclusion: In this large prospective study, high serum

β

-carotene concentrations were associated with increased risk for aggressive, clinically relevant prostate cancer. Lycopene and other carotenoids were unrelated to prostate cancer. Consistent with other recent publications, these results suggest that lycopene or tomato-based regimens will not be effective for prostate cancer prevention.

(Cancer Epidemiol Biomarkers Prev 2007;16(5):962-8), "DOI": "10.1158/1055-9965.EPI-06-0861", "journalAbbreviation": "Cancer Epidemiol Biomarkers Prev", "author": [{"family": "Peters", "given": "Ulrike"}, {"family": "Leitzmann", "given": "Michael F."}, {"family": "Chatterjee", "given": "Nilanjan"}, {"family": "Wang", "given": "Yinghui"}, {"family": "Albanes", "given": "Demetrius"}, {"family": "Germann", "given": "Edward P."}, {"family": "Friesen", "given": "Marlin D."}, {"family": "Riboli", "given": "Elio"}, {"family": "Hayes", "given": "Richard B."}], "issued": {"date-parts": [{"2007", 5, 1}]}, {"id": "776", "uris": [{"http://zotero.org/users/2724931/items/QIHKN2VR"}], "uri": [{"http://zotero.org/users/2724931/items/QIHKN2VR"}], "itemData": {"id": "776", "type": "article-journal", "title": "Plasma and Dietary Carotenoids, and the Risk of Prostate Cancer", "container-title": "Cancer Epidemiology Biomarkers & Prevention", "page": "260", "volume": "13", "issue": "2", "abstract": "The association between plasma carotenoids and prostate cancer risk was investigated in a case-control study nested within the prospective Health Professionals Follow-up Study. We matched 450 incident prostate cancer cases diagnosed from 1993-1998 to 450 controls by age, time, month, and year of blood donation. Modest inverse, but not statistically significant, associations were observed among plasma

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-carotene, and lycopene concentrations, and overall risk of prostate cancer diagnosis {odds ratio (highest versus lowest quintile; OR), α

-carotene: OR, 0.67 [95% confidence interval (CI), -0.40-1.09]; β

-carotene: OR, 0.78 (95% CI, 0.48-1.25); lycopene: OR, 0.66 (95% CI, 0.38-1.13)). The inverse association between plasma lycopene concentrations and prostate cancer risk was limited to participants who were 65 years or older (OR, 0.47; 95% CI, 0.23-0.98) and without a family history of prostate cancer (OR, 0.48; 95% CI, 0.26-0.89). Combining, older age and a negative family history provided similar results (OR, 0.43; 95% CI, 0.18-1.02). Inverse associations between β

-carotene and prostate cancer risk were also found among younger participants (<65 years of age; OR, 0.36; 95% CI, 0.14-0.91; P trend = 0.03). Combining dietary intake and plasma data confirmed our results. We found a statistically significant inverse association between higher plasma lycopene concentrations and lower risk of prostate cancer, which was restricted to older participants and those without a family history of prostate cancer. This observation suggests that tomato products may exhibit more potent protection against sporadic prostate cancer rather than those with a stronger familial or hereditary component. In addition, our findings also suggest that among younger men, diets rich in β

-carotene may also play a protective role in prostate carcinogenesis.", "DOI": "10.1158/1055-9965.EPI-03-0012", "journalAbbreviation": "Cancer Epidemiol Biomarkers Prev", "author": [{"family": "Wu", "given": "Kana"}, {"family": "Erdman", "given": "John W."}, {"family": "Schwartz", "given": "Steven J."}, {"family": "Platz", "given": "Elizabeth A."}, {"family": "Leitzmann", "given": "Michael"}, {"family": "Clinton", "given": "Steven K."}, {"family": "DeGroot", "given": "Valerie"}, {"family": "Willett", "given": "Walter C."}, {"family": "Giovannucci", "given": "Edward"}], "issued": {"date-parts": [{"2004", 2, 1}]}, {"id": "772", "uris": [{"http://zotero.org/users/2724931/items/Z88XYJCK"}], "uri": [{"http://zotero.org/users/2724931/items/Z88XYJCK"}], "itemData": {"id": "772", "type": "article-journal", "title": "Associations Between Circulating Carotenoids, Genomic Instability and the Risk of High-Grade Prostate Cancer", "container-title": "The Prostate", "page": "339-348", "volume": "76", "issue": "4", "archive": "PMC", "archive_location": "PMC5493324", "abstract": "BACKGROUND Carotenoids are a class of nutrients with antioxidant properties that have been purported to protect against cancer. However, the reported associations between carotenoids and prostate cancer have been heterogeneous and lacking data on interactions with nucleotide sequence variations and genomic biomarkers. OBJECTIVE: To examine the associations between carotenoid levels and the risk of high-grade prostate cancer, also considering antioxidant-related genes and tumor instability. METHODS: We measured plasma levels of carotenoids and genotyped 20 single nucleotide polymorphisms (SNP) in SOD1, SOD2, SOD3, XRCC1, and OGG1 among 559 men with non-metastatic prostate cancer undergoing radical prostatectomy. We performed copy number analysis in a subset of these men (n = 67) to study tumor instability assessed as Fraction of the Genome Altered (FGA). We examined associations between carotenoids, genotypes, tumor instability and risk of high-grade prostate cancer (Gleason grade $\geq 4 + 3$) using logistic and linear regression. RESULTS: Circulating carotenoid levels were inversely associated with the risk of high-grade prostate cancer; odds ratios (OR) and 95% confidence intervals (CI) comparing highest versus lowest quartiles were: 0.34 (95% CI: 0.18-0.66) for α

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-carotene and lycopene and their major plant food sources, including carrots, green leafy vegetables, and tomato-based foods. The study was carried out in Auckland, New Zealand, during 1996–1997 and recruited 317 prostate cancer cases and 480 controls. The authors found that dietary intake of

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-carotene and its main vegetable sources was largely unassociated with prostate cancer risk, whereas intake of lycopene and tomato-based foods was weakly associated with a reduced risk. These results suggest that in contrast to the findings regarding many types of cancers, vegetables rich in

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-carotene are not protective against prostate cancer. However, lycopene from tomato-based foods was found to be associated with a small reduction in risk. Am J Epidemiol 2000; 151:119–

23. ", "DOI": "10.1093/oxfordjournals.aje.a010176", "ISSN": "0002-9262", "journalAbbreviation": "American Journal of Epidemiology", "author": [{"family": "Norris", "given": "Alan E."}, {"family": "Jackson", "given": "Rodney T."}, {"family": "Sharpe", "given": "Susan J."}, {"family": "Skeaff", "given": "C. Murray"}], "issued": {"date-parts": [{"2000", 1, 15}]}}, {"id": "760", "uris": [{"http://zotero.org/users/2724931/items/2YX9MMBA"}], "uri": [{"http://zotero.org/users/2724931/items/2YX9MMBA"}], "itemData": {"id": "760", "type": "article-journal", "title": "Retinol, carotenoids and the risk of prostate cancer: A case-control study from Italy", "container-title": "International Journal of Cancer", "page": "689-692", "volume": "112", "issue": "4", "abstract": "Abstract Several studies have evaluated the possible association between intakes of retinoids and carotenoids and the risk of prostate cancer, but the evidence is still inconsistent. Further, only a few studies have investigated the role of specific carotenoids other than β -carotene. We have thus considered the association between retinol and various carotenoids using data from a multicentric case-control study conducted in Italy between 1991 and 2002. This included 1,294 incident, histologically confirmed prostate cancer cases below age 75 years admitted to major teaching and general hospitals in the areas under study, and 1,451 controls below age 75 years selected among patients admitted to the same hospitals as cases for a wide spectrum of acute nonneoplastic conditions not related to long-term modifications of diet. Subjects' usual diet was investigated by means of a validated food-frequency questionnaire. Multivariate odds ratios and the corresponding 95% confidence intervals were estimated using unconditional logistic regression models. The risk of prostate cancer tended to decrease with increasing intake of retinol (OR = 0.79 for the highest versus the lowest quintile of intake), carotene (OR = 0.70),

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-carotene (OR = 0.85) and β -carotene (OR = 0.72), although the estimates were significant for carotene and β -carotene only. No meaningful associations emerged for nonprovitamin A carotenoids, such as lycopene (OR = 0.94) and lutein/zeaxanthin (OR = 0.91). No systematic heterogeneity was observed across strata of age, education and body mass index. Thus, our study supports the hypothesis of a weak protective effect of carotene, particularly β -carotene, on the risk of prostate cancer, while it indicates that other carotenoids, including lycopene, and retinol are not appreciably related to the risk of this neoplasm. © 2004 Wiley-Liss,

Inc.", "DOI": "10.1002/ijc.20486", "ISSN": "0020-7136", "journalAbbreviation": "International Journal of Cancer", "author": [{"family": "Bosetti", "given": "Cristina"}, {"family": "Talamini", "given": "Renato"}, {"family": "Montella", "given": "Maurizio"}, {"family": "Negri", "given": "Eva"}, {"family": "Conti", "given": "Ettore"}, {"family": "Franceschi", "given": "Silvia"}, {"family": "La Vecchia", "given": "Carlo"}], "issued": {"date-parts": [{"2004", 7, 9}]}}, {"id": "770", "uris": [{"http://zotero.org/users/2724931/items/VCIH4USS"}], "uri": [{"http://zotero.org/users/2724931/items/VCIH4USS"}], "itemData": {"id": "770", "type": "article-journal", "title": "A case-control study of diet and prostate cancer.", "container-title": "British Journal of Cancer", "page": "678-687", "volume": "76", "issue": "5", "archive": "PMC", "archive_location": "PMC2228001", "abstract": "We interviewed 328 men diagnosed with prostate cancer before the age of 75 years and 328 age-matched population controls. The principal hypotheses were that risk would increase with a high intake of total or saturated fat and would decrease with a high intake of carotene (beta-carotene equivalents) or lycopene. We also examined the associations of other nutrients and foods with risk. There was no evidence for an association between fat intake and risk, although the average fat intake was high and the range of fat intakes was narrow (medians of lower and upper thirds of percentage of energy from fat among controls were 34.3% and 42.9% respectively). Risk was lower in subjects with higher carotene intake: odds ratios 0.65 (95% CI 0.45-0.94) and 0.76 (0.53-1.10) in the middle and upper thirds of carotene intake respectively (P for trend = 0.150). Lycopene was not associated with risk. Among 13 other nutrients examined, the odds ratios in the top third of intake were below 0.8 for: potassium, 0.74 (0.51-1.09; P for trend = 0.054); zinc, 0.73 (0.49-1.08; P for trend = 0.126); iodine, 0.75 (0.51-1.11; P for trend = 0.077); vitamin B6 food only, 0.77 (0.53-1.12; P for trend = 0.077); and vitamin B6 including supplements, 0.70 (0.48-1.03; P for trend = 0.029). Among 18 foods examined, statistically significant associations were observed for: garlic as food, > or = 2/week vs never, 0.56 (0.33-0.93); garlic including supplements, > or = 2/week vs never, 0.60 (0.37-0.96); baked beans, > or = 2/week vs < 1/month, 0.57 (0.34-0.95); and garden peas, > or = 5/week vs < or = 3/month, 0.35 (0.13-0.91). This study does not support the hypothesis that fat increases risk and is equivocal in relation to carotene. The possible relationships of vitamin B6, garlic, beans and peas with risk for prostate cancer should be further investigated.", "ISSN": "0007-0920", "author": [{"family": "Key", "given": "T J"}, {"family": "Silcocks", "given": "P B"}, {"family": "Davey", "given": "G K"}, {"family": "Appleby", "given": "P N"}, {"family": "Bishop", "given": "D T"}], "issued": {"date-parts": [{"1997"}]}}, {"id": "768", "uris": [{"http://zotero.org/users/2724931/items/84P4HPA6"}], "uri": [{"http://zotero.org/users/2724931/items/84P4HPA6"}], "itemData": {"id": "768", "type": "article-journal", "title": "Do dietary lycopene and other carotenoids protect against prostate cancer?", "container-title": "International Journal of Cancer", "page": "1010-1014", "volume": "113", "issue": "6", "abstract": "Abstract To determine whether dietary intake of lycopene and other carotenoids has an etiological association with prostate cancer, a case-control study was conducted in Hangzhou, southeast China during 2001-2002. The cases were 130 incident patients with histologically confirmed adenocarcinoma of the prostate. The controls were 274 hospital inpatients without prostate cancer or any other malignant diseases. Information on usual food consumption, including vegetables and fruits, was collected by face-to-face interviews using a structured food frequency questionnaire. The risks of prostate cancer for the intake of carotenoids and selected vegetables and fruits rich in carotenoids were assessed using multivariate logistic regression, adjusting for age, locality, education, income, body mass index, marital status, number of children, family history of prostate cancer, tea drinking, total fat and caloric intake. The prostate cancer risk declined with increasing consumption of lycopene,

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-carotene, β -carotene, β -cryptoxanthin, lutein and zeaxanthin. Intake of tomatoes, pumpkin, spinach, watermelon and citrus fruits were also inversely associated with the prostate cancer risk. The adjusted odds ratios for the highest versus the lowest quartiles of intake were 0.18 (95% CI: 0.08-0.41) for lycopene, 0.43 (95% CI: 0.21-0.85) for

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-carotene, 0.34 (95% CI: 0.17-0.69) for β -carotene, 0.15 (95% CI: 0.06-0.34) for β -cryptoxanthin and 0.02 (95% CI: 0.01-0.10) for lutein and zeaxanthin. The corresponding dose-response relationships were also significant, suggesting that vegetables and fruits rich in lycopene and other carotenoids may be protective against prostate cancer. © 2004 Wiley-Liss, Inc., "DOI": "10.1002/ijc.20667", "ISSN": "0020-7136", "journalAbbreviation": "International Journal of Cancer", "author": [{"family": "Jian", "given": "Le"}, {"family": "Du", "given": "Chuan-Jun"}, {"family": "Lee", "given": "Andy H."}, {"family": "Binns", "given": "Colin W."}], "issued": {"date-parts": ["2004", 10, 28]}}, "schema": "https://github.com/citation-style-language/schema/raw/master/csl-citation.json"}
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-tocopherol were lower for lung cancer cases than controls. Statistically significant trends across quartiles were observed in lutein ($P = 0.02$), zeaxanthin ($P = 0.02$), and

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-tocopherol ($P = 0.03$). The carotenoid findings in the overall population were because of the strong inverse association between serum micronutrients and lung cancer in females. Statistically significant odds ratios (ORs) comparing 4th to 1st quartiles in the female population were seen in lutein [OR, 0.31; confidence interval (CI), 0.13–0.75], zeaxanthin (OR, 0.31; CI, 0.12–0.77), and

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-cryptoxanthin (OR, 0.34; CI, 0.14–0.81). For prostate cancer, mean serum concentrations were lower in cases for all of the nutrients except

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-carotene. Only for

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-tocopherol ($P_{trend} = 0.04$) were the findings statistically significant. There was no statistically significant association between serum carotenoids and prostate cancer. Our findings provide additional support for the association between physiological levels of dietary micronutrients and cancer incidence. {"family": "Goodman", "given": "Gary E."}, {"family": "Schaffer", "given": "Steven"}, {"family": "Omenn", "given": "Gilbert S."}, {"family": "Chen", "given": "Chu"}, {"family": "King", "given": "Irena"}, {"issued": [{"date-parts": [{"2003", 6, 1]}]}, {"id": "775", "uris": ["http://zotero.org/users/2724931/items/6GDCVHDT"], "uri": ["http://zotero.org/users/2724931/items/6GDCVHDT"], "itemData": {"id": "775", "type": "article-journal", "title": "Serum Lycopene, Other Carotenoids, and Prostate Cancer Risk: a Nested Case-Control Study in the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial", "container-title": "Cancer Epidemiology Biomarkers & Prevention", "page": "962", "volume": "16", "issue": "5", "abstract": "Background: Reports from several studies have suggested that carotenoids, and in particular lycopene, could be prostate cancer-preventive agents. This has stimulated extensive laboratory and clinical research, as well as much commercial and public enthusiasm. However, the epidemiologic evidence remains inconclusive. Materials and Methods: We investigated the association between prediagnostic serum carotenoids (lycopene,

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-cryptoxanthin, lutein, and zeaxanthin) and risk of prostate cancer in the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial, a multicenter study designed to examine methods of early detection and risk factors for cancer. The study included 692 incident prostate cancer cases, diagnosed 1 to 8 years after study entry, including 270 aggressive cases, with regional or distant stage ($n = 90$) or Gleason score ≥ 7 ($n = 235$), and 844 randomly selected, matched controls. As study participants were selected from those who were assigned to annual standardized screening for prostate cancer, results are unlikely to be biased by differential screening, a circumstance that is difficult to attain under non-trial conditions. Results: No association was observed between serum lycopene and total prostate cancer [odds ratios (OR), 1.14; 95% confidence intervals (95% CI), 0.82–1.58 for highest versus lowest quintile; P for trend, 0.28] or aggressive prostate cancer (OR, 0.99; 95% CI, 0.62–1.57 for highest versus lowest quintile; P for trend, 0.433).

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-Carotene was associated with an increased risk of aggressive prostate cancer (OR, 1.67; 95% CI, 1.03–2.72 for highest versus lowest quintile; P for trend, 0.13); in particular, regional or distant stage disease (OR, 3.16; 95% CI, 1.37–7.31 for highest versus lowest quintile; P for trend, 0.02); other carotenoids were not associated with risk. Conclusion: In this large prospective study, high serum

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-carotene concentrations were associated with increased risk for aggressive, clinically relevant prostate cancer. Lycopene and other carotenoids were unrelated to prostate cancer. Consistent with other recent publications, these results suggest that lycopene or tomato-based regimens will not be effective for prostate cancer prevention. (Cancer Epidemiol Biomarkers Prev 2007;16(5):962–8), "DOI": "10.1158/1055-9965.EPI-06-0861", "journalAbbreviation": "Cancer Epidemiol Biomarkers Prev", "author": [{"family": "Peters", "given": "Ulrike"}, {"family": "Leitzmann", "given": "Michael F."}, {"family": "Chatterjee", "given": "Nilanjan"}, {"family": "Wang", "given": "Yinghui"}, {"family": "Albanes", "given": "Demetrios"}, {"family": "Germann", "given": "Edward P."}, {"family": "Friesen", "given": "Marlin D."}, {"family": "Riboli", "given": "Elio"}, {"family": "Hayes", "given": "Richard B."}], "issued": [{"date-parts": [{"2007", 5, 1]}]}, {"id": "771", "uris": ["http://zotero.org/users/2724931/items/XXKA5QES"], "uri": ["http://zotero.org/users/2724931/items/XXKA5QES"], "itemData": {"id": "771", "type": "article-journal", "title": "A Prospective Study of Lycopene and Tomato Product Intake and Risk of Prostate Cancer", "container-title": "Cancer Epidemiology Biomarkers & Prevention", "page": "92", "volume": "15", "issue": "1", "abstract": "Background: Dietary lycopene and tomato products may reduce risk of prostate cancer; however, uncertainty remains about this possible association. Methods: We evaluated the association between intake of lycopene and specific tomato products and prostate cancer risk in the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial, a multicenter study designed to investigate cancer early detection methods and etiologic determinants. Participants completed both a general risk factor and a 137-item food frequency questionnaire at baseline. A total of 1,338 cases of prostate cancer were identified among 29,361 men during an average of 4.2 years of follow-up. Results: Lycopene intake was not associated with prostate cancer risk. Reduced risks were also not found for total tomato servings or for most tomato-based foods. Statistically nonsignificant inverse associations were noted for pizza [all prostate cancer: relative risk (RR), 0.83; 95% confidence interval (95% CI), 0.67–1.03 for ≥ 1 serving/wk versus < 0.5 serving/mo; $P_{trend} = 0.06$ and advanced prostate cancer: RR, 0.79; 95% CI, 0.56–1.10; $P_{trend} = 0.12$] and spaghetti/tomato sauce consumption (advanced prostate cancer: RR = 0.81, 95% CI, 0.57–1.16 for ≥ 2 servings/wk versus < 1 serving/mo; $P_{trend} = 0.31$). Among men with a family history of prostate cancer, risks were decreased in relation to increased consumption of lycopene ($P_{trend} = 0.04$) and specific tomato-based foods commonly eaten with fat (spaghetti, $P_{trend} = 0.12$; pizza, $P_{trend} = 0.15$; lasagna, $P_{trend} = 0.02$). Conclusions: This large study does not support the hypothesis that greater lycopene/tomato product consumption protects from prostate cancer. Evidence for protective associations in subjects with a family history of prostate cancer requires further corroboration. (Cancer Epidemiol Biomarkers Prev 2006;15(1):92–8), "DOI": "10.1158/1055-9965.EPI-05-0563", "journalAbbreviation": "Cancer Epidemiol Biomarkers Prev", "author":

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David"}, {"family": "Hayes", "given": "Richard B."}], [{"date-parts": [{"2006", 1, 1}]}], [{"id": 759, "uris": ["http://zotero.org/users/2724931/items/UC8EM9WV"], "uri": ["http://zotero.org/users/2724931/items/UC8EM9WV"], "itemData": {"id": 759, "type": "article-journal", "title": "Serum levels of folate, lycopene, β -carotene, retinol and vitamin E and prostate cancer risk", "container-title": "European Journal Of Clinical Nutrition", "page": "1235", "volume": "64", "journalAbbreviation": "European Journal Of Clinical Nutrition", "author": [{"family": "Beilby", "given": "J"}, {"family": "Ambrosini", "given": "G L"}, {"family": "Rossi", "given": "E"}, {"family": "Klerk", "given": "N H", "non-dropping-particle": "de"}, {"family": "Musk", "given": "A W"}], [{"date-parts": [{"2010", 8, 4}]}], [{"id": 773, "uris": ["http://zotero.org/users/2724931/items/M8ZPITDZ"], "uri": ["http://zotero.org/users/2724931/items/M8ZPITDZ"], "itemData": {"id": 773, "type": "article-journal", "title": "Prostate Cancer and Dietary Carotenoids", "container-title": "American Journal of Epidemiology", "page": "119-123", "volume": "151", "issue": "2", "abstract": "This population-based case-control study investigated associations between prostate cancer risk and dietary intake of the carotenoids β -carotene and lycopene and their major plant food sources, including carrots, green leafy vegetables, and tomato-based foods. The study was carried out in Auckland, New Zealand, during 1996–1997 and recruited 317 prostate cancer cases and 480 controls. The authors found that dietary intake of β -carotene and its main vegetable sources was largely unassociated with prostate cancer risk, whereas intake of lycopene and tomato-based foods was weakly associated with a reduced risk. These results suggest that in contrast to the findings regarding many types of cancers, vegetables rich in β -carotene are not protective against prostate cancer. However, lycopene from tomato-based foods was found to be associated with a small reduction in risk. Am J Epidemiol 2000; 151:119-23."}], [{"DOI": "10.1093/oxfordjournals.aje.a010176", "ISSN": "0002-9262", "journalAbbreviation": "American Journal of Epidemiology", "author": [{"family": "Norris", "given": "Alan E."}, {"family": "Jackson", "given": "Rodney T."}, {"family": "Sharpe", "given": "Susan J."}, {"family": "Skeaff", "given": "C. Murray"}], [{"date-parts": [{"2000", 1, 15}]}], [{"id": 760, "uris": ["http://zotero.org/users/2724931/items/2YX9MMBA"], "uri": ["http://zotero.org/users/2724931/items/2YX9MMBA"], "itemData": {"id": 760, "type": "article-journal", "title": "Retinol, carotenoids and the risk of prostate cancer: A case-control study from Italy", "container-title": "International Journal of Cancer", "page": "689-692", "volume": "112", "issue": "4", "abstract": "Abstract Several studies have evaluated the possible association between intakes of retinoids and carotenoids and the risk of prostate cancer, but the evidence is still inconsistent. Further, only a few studies have investigated the role of specific carotenoids other than β -carotene. We have thus considered the association between retinol and various carotenoids using data from a multicentric case-control study conducted in Italy between 1991 and 2002. 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α

-carotene, β -carotene, β -cryptoxanthin, lutein and zeaxanthin. Intake of tomatoes, pumpkin, spinach, watermelon and citrus fruits were also inversely associated with the prostate cancer risk. The adjusted odds ratios for the highest versus the lowest quartiles of intake were 0.18 (95% CI: 0.08-0.41) for lycopene, 0.43 (95% CI: 0.21-0.85) for

α

-carotene, 0.34 (95% CI: 0.17-0.69) for β -carotene, 0.15 (95% CI: 0.06-0.34) for β -cryptoxanthin and 0.02 (95% CI: 0.01-0.10) for lutein and zeaxanthin. The corresponding dose-response relationships were also significant, suggesting that vegetables and fruits rich in lycopene and other carotenoids may be protective against prostate cancer. ? 2004 Wiley-Liss, Inc., "DOI": "10.1002/ijc.20667", "ISSN": "0020-7136", "journalAbbreviation": "International Journal of Cancer", "author": [{"family": "Jian", "given": "Le"}, {"family": "Du", "given": "Chuan-Jun"}, {"family": "Lee", "given": "Andy H."}, {"family": "Binns", "given": "Colin W."}], "issued": {"date-parts": [{"2004", 10, 28}]}, {"schema": "https://github.com/citation-style-language/schema/raw/master/csl-citation.json"}
22, 32, 34

]

RE

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1.10

(

P

= 0.27)

82

0.28

16.37, df = 3

(

P

= 0.0010)

Study Center

3 (3)

[

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β

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β

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β

-cryptoxanthin,

α

-carotene,

α

-tocopherol, retinol, and retinyl palmitate reaching statistical significance at $P = 0.05$. In the overall population, the mean serum concentrations of all of the micronutrients except

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β

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α

-carotene,

β

-carotene,

β

-cryptoxanthin, lutein, and zeaxanthin) and risk of prostate cancer in the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial, a multicenter study designed to examine methods of early detection and risk factors for cancer. The study included 692 incident prostate cancer cases, diagnosed 1 to 8 years after study entry, including 270 aggressive cases, with regional or distant stage ($n = 90$) or Gleason score ≥ 7 ($n = 235$), and 844 randomly selected, matched controls. As study participants were selected from those who were assigned to annual standardized screening for prostate cancer, results are unlikely to be biased by differential screening, a circumstance that is difficult to attain under non-trial conditions. Results: No association was observed between serum lycopene and total prostate cancer [odds ratios (OR), 1.14; 95% confidence intervals (95% CI), 0.82-1.58 for highest versus lowest quintile; P for trend, 0.28] or aggressive prostate cancer (OR, 0.99; 95% CI, 0.62-1.57 for highest versus lowest quintile; P for trend, 0.433).

β

-Carotene was associated with an increased risk of aggressive prostate cancer (OR, 1.67; 95% CI, 1.03-2.72 for highest versus lowest quintile; P for trend, 0.13); in particular, regional or distant stage disease (OR, 3.16; 95% CI, 1.37-7.31 for highest versus lowest quintile; P for trend, 0.02); other carotenoids were not associated with risk. Conclusion: In this large prospective study, high serum

β

-carotene concentrations were associated with increased risk for aggressive, clinically relevant prostate cancer. Lycopene and other carotenoids were unrelated to prostate cancer. Consistent with other recent publications, these results suggest that lycopene or tomato-based regimens will not be effective for prostate cancer prevention.

(Cancer Epidemiol Biomarkers Prev 2007;16(5):962-8),"DOI":"10.1158/1055-9965.EPI-06-0861","journalAbbreviation":"Cancer Epidemiol Biomarkers Prev","author":[{"family":"Peters","given":"Ulrike"}, {"family":"Leitzmann","given":"Michael F."}, {"family":"Chatterjee","given":"Nilanjan"}, {"family":"Wang","given":"Yinghui"}, {"family":"Albanes","given":"Demetrius"}, {"family":"Germann","given":"Edward P."}, {"family":"Friesen","given":"Marlin D."}, {"family":"Riboli","given":"Elio"}, {"family":"Hayes","given":"Richard B."}], "issued":{"date-parts":["2007",5,1]}}, {"id":760,"uris":["http://zotero.org/users/2724931/items/2YX9MMBA"],"uri":["http://zotero.org/users/2724931/items/2YX9MMBA"],"itemData":{"id":760,"type":"article-journal","title":"Retinol, carotenoids and the risk of prostate cancer: A case-control study from Italy","container-title":"International Journal of Cancer","page":"689-692","volume":"112","issue":"4","abstract":"Abstract Several studies have evaluated the possible association between intakes of retinoids and carotenoids and the risk of prostate cancer, but the evidence is still inconsistent. Further, only a few studies have investigated the role of specific carotenoids other than β -carotene. We have thus considered the association between retinol and various carotenoids using data from a multicentric case-control study conducted in Italy between 1991 and 2002. This included 1,294 incident, histologically confirmed prostate cancer cases below age 75 years admitted to major teaching and general hospitals in the areas under study, and 1,451 controls below age 75 years selected among patients admitted to the same hospitals as cases for a wide spectrum of acute nonneoplastic conditions not related to long-term modifications of diet. Subjects' usual diet was investigated by means of a validated food-frequency questionnaire. Multivariate odds ratios and the corresponding 95% confidence intervals were estimated using unconditional logistic regression models. The risk of prostate cancer tended to decrease with increasing intake of retinol (OR = 0.79 for the highest versus the lowest quintile of intake), carotene (OR = 0.70),

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23, 24, 32

]

FE

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0.16

(

P

= 0.87)

0

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(

P

= 0.67)

Smoking

2 (2)

[

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α

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β

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β

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β

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]

FE

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0.96

(

P

= 0.34)

28

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P

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Height

2 (2)

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β
-carotene and lycopene and their major plant food sources, including carrots, green leafy vegetables, and tomato-
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cancer cases and 480 controls. The authors found that dietary intake of
β
-carotene and its main vegetable sources was largely unassociated with prostate cancer risk, whereas intake of
lycopene and tomato-based foods was weakly associated with a reduced risk. These results suggest that in contrast
to the findings regarding many types of cancers, vegetables rich in
β
-carotene are not protective against prostate cancer. However, lycopene from tomato-based foods was found to be
associated with a small reduction in risk. Am J Epidemiol 2000; 151:119-
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1.91
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P
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Caloric intake
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dietary lycopene and other carotenoids protect against prostate cancer?","container-title":"International Journal of
Cancer","page":"1010-1014","volume":"113","issue":"6","abstract":"Abstract To determine whether dietary intake
of lycopene and other carotenoids has an etiological association with prostate cancer, a case?control study was
conducted in Hangzhou, southeast China during 2001?2002. The cases were 130 incident patients with
histologically confirmed adenocarcinoma of the prostate. The controls were 274 hospital inpatients without
prostate cancer or any other malignant diseases. Information on usual food consumption, including vegetables and
fruits, was collected by face-to-face interviews using a structured food frequency questionnaire. The risks of
prostate cancer for the intake of carotenoids and selected vegetables and fruits rich in carotenoids were assessed
using multivariate logistic regression, adjusting for age, locality, education, income, body mass index, marital

```

status, number of children, family history of prostate cancer, tea drinking, total fat and caloric intake. The prostate cancer risk declined with increasing consumption of lycopene,

α

-carotene, β -carotene, β -cryptoxanthin, lutein and zeaxanthin. Intake of tomatoes, pumpkin, spinach, watermelon and citrus fruits were also inversely associated with the prostate cancer risk. The adjusted odds ratios for the highest versus the lowest quartiles of intake were 0.18 (95% CI: 0.08-0.41) for lycopene, 0.43 (95% CI: 0.21-0.85) for

α

-carotene, 0.34 (95% CI: 0.17-0.69) for β -carotene, 0.15 (95% CI: 0.06-0.34) for β -cryptoxanthin and 0.02 (95% CI: 0.01-0.10) for lutein and zeaxanthin. The corresponding dose-response relationships were also significant, suggesting that vegetables and fruits rich in lycopene and other carotenoids may be protective against prostate cancer. © 2004 Wiley-Liss, Inc., "DOI": "10.1002/ijc.20667", "ISSN": "0020-7136", "JournalAbbreviation": "International Journal of Cancer", "author": [{"family": "Jian", "given": "Le"}, {"family": "Du", "given": "Chuan-Jun"}, {"family": "Lee", "given": "Andy H."}, {"family": "Binns", "given": "Colin W."}], "issued": {"date-parts": ["2004", "10", "28"]}], "schema": "https://github.com/citation-style-language/schema/raw/master/csl-citation.json"}
32, 34

]

RE

0.43 [0.09, 2.17]

1.02

(

P

= 0.31)

93

1.27

13.99, df = 1 (

P

= 0.0002)

BMI

Body mass

index

,

df

degree of freedom

, FE

fixed effects

, N/A

not-applicable

, PC

prostate cancer

, OR

odds ratio

, RE

random effects

.

Figure

SEQ Figure * ARABIC

2

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Forest plot for the association between Carotenoids and PC risk

Lutein/Zeaxanthin

Aiming

to investigate the relationship between lutein/zeaxanthin and PC risk, the summary of ORs of six case-control studies with nine datasets was estimated. We observed a statistically non-significant decrease in PC risk

with an OR of 0.86 (95% CI 0.64-1.15) with high heterogeneity ($I^2 = 72\%$). A slight decrease and yet statistically not-significant was noticed within North American populations and for studies using serum concentrations of lutein/zeaxanthin to investigate the association (OR = 0.96; 95% CI 0.81-1.14).

β -cryptoxanthin

In a pooled analysis of six case-control studies reporting data about the effect of

β

-cryptoxanthin on PC risk, an OR of 0.80 (95% CI 0.58-1.09, $I^2 = 70\%$) was found, indicating a statistically non-significant inverse association. A slight decrease and yet statistically not-significant was noticed within North American populations and for studies using serum concentrations of

β

-cryptoxanthin to investigate the association (OR = 0.98; 95% CI 0.80-1.20).

Publication bias

The funnel plots

put

in the Supplementary figures show no sign of asymmetry. Among the five meta-analyses, the risk of bias assessment was available for two analyses since they included a number of datasets ≥ 10 . Both analyses showed no evidence of small study effect. The analysis of lycopene and PC (Begg's test $P = 0.9605$, Egger's test $P = 0.678$) and the analysis of

β

-Carotene and PC (Begg's test $P = 0.216$, Egger's test $P = 0.522$).

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DISCUSSION

The current meta-analysis, which included 13 studies, provided evidence that carotenoids could prevent against PC. To sum up, the overall analysis demonstrated a significant decrease in PC incidence. The same pattern was noticed for all types of carotenoids investigated in our study i.e. lycopene

β -carotene,
 α -carotene,
 β -cryptoxanthin, and lutein/zeaxanthin.
 In vitro and animal
 ,
 studies have provided evidence that carotenoids may protect against several types of cancer [

 31
 –
 34
]. Additionally, the World Cancer Research Fund (WCRF) released a comprehensive report on food and cancer prevention in 2007
 highlighting that foods containing carotenoids are probably protective against lung, mouth, pharynx, and larynx cancers [

 35
].
 Stahl and
 Sies
 [

 36
] stated that carotenoids and/or their metabolites influence the expression of certain genes or may act as regulatory enzymes inhibitors
 in context with cancer preventive properties of these compounds.
 The mechanism underlying the beneficial effect of lycopene on PC risk can be explained by this carotenoid high biological activity
 through antioxidant properties as preventing DNA damage by scavenging free radicals [

 8
] and modulating gene expression related to PC growth [

 37
]. Furthermore, Yang
 et al.
 , [

 38
] showed that this non-provitamin A carotenoid inhibits PC cell proliferation via the
 PPAR
 Y
 -LXR
 α
 – ABCA1 pathway. According to Stahl and
 Sies
 [

 36
] and
 Gerster
 [

 3
 9
], lycopene was found to hamper the progression of PC via apoptosis induction and angiogenesis suppression.
 The current analysis provides support for future studies using carotenoid-based dietary or supplementation interventions and plays a
 key role in PC survivorship including treatment.
 Concerning the risk of PC, our results agree with some previous studies. Wang
 et al
 . [

 40
], reported in a meta-analysis of 34 studies, that lycopene (RR = 0.88; 95% CI 0.76-1.02), but not
 β -carotene (RR = 0.90; 95% CI 0.81-1.01), were inversely associated with the risk of PC.
 Nonetheless, both Chen
 et al
 . (2015) [

 41
],
 Ilic
 et al
 . [

 42
] found a positive association between lycopene consumption (RR
 = 0.91; 95% CI 0.81-1.01) and (OR = -
 0.34; 95% CI -
 2.01-1.32) respectively with the risk of PC.
 Controversially to our analysis, Wang
 et al
 . [

 40
] stated that
 α -carotene (RR = 0.87; 95% CI 0.76-0.99) was positively associated with the risk of developing PC.
 However, similar to dietary carotene intake, Van Hoang
 et al
 . [

 43
] observed in a case-control study no relationship between
 β

-cryptoxanthin intake as well as lutein and zeaxanthin with adjusted ORs of 1.29 (95% CI 0.79-2.09) and 0.73 (95% CI 0.44-1.20) respectively with PC risk.

The type of studies (cohort and case-control), populations (Asia, Europe, Australia, and the USA) slightly influenced the odds estimate. However, sensitivity analysis further showed that when omitting the studies conducted by (Jian et al

., 2004) [

30

], the results noticeably changed.

To the best of our knowledge, this is the first meta-analysis undertaken to highlight the relationship between carotenoids and PC risk.

However, some limitations should be considered as the limited number of articles included in

our analysis. Moreover, our analyses showed heterogeneity evidence. However, subgroup analysis demonstrated sources of heterogeneity

that

could be attributable to including different study designs in the analyses.

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CONCLUSION

The current meta-analysis has been undertaken to assess available evidence for treatment and prevention of PC, to show the contribution of carotenoids, their intake or supplementation, and to perform a comparison between their relationships with PC risk.

Our results showed that all types of carotenoids investigated in our study may contribute to the prevention of PC. To determine whether they are clinically relevant, more laboratory and clinical trials are needed on the effects of these compounds on the behavior of prostate cancer cells and tissues. Moreover, the lack of evidence and data supports the call for publishing more research in this area to investigate the effectiveness of carotenoids for the prevention and treatment of PC.

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