

Literaturverzeichnis nach Kapiteln

(Stand 12/2018)

Vorbemerkung.....

Das Literaturverzeichnis zum Kitteltaschenbuch Fettstoffwechsel dient einer möglichen Vertiefung der im Kitteltaschenbuch beschriebenen Inhalte und führt Original- bzw. Studien- oder zusammenfassende Sekundärliteratur zu den einzelnen Kapiteln auf oder Literatur die praxisnahe Ergebnisse und Hilfestellungen leistet.

Wichtige Leitlinien sind den jeweiligen Kapiteln vorangestellt.

In Übersichtsartikeln und Reviews wird die recherchierte Originalliteratur zitiert, die in der Regel aber einem kostenpflichtigen Zugang (z.B. im Internet über die Homepage eines Verlags oder einer Fachzeitschrift) unterliegt.

Wenn die zitierte Literatur über das Internet direkt zugänglich ist, sind die entsprechenden Links angegeben; dort lassen sich die Artikel einsehen oder auch downloaden.

Zur Literatur mit Links aus dem Internet wird in Klammern normalerweise das letzte Datum der für diese Zusammenstellung erfolgten Einsicht angegeben. Hier erfolgte die letzte Prüfung aller Links am 10. November 2017.

Fassungen der Nationalen Versorgungsleitlinien sind über das Portal „Versorgungsleitlinien“ zugänglich. Das Programm für die Nationalen Versorgungsleitlinien ist eine Initiative von BÄK, KBV und AWMF (siehe nächster Absatz) zur Qualitätsförderung in der Medizin (www.versorgungsleitlinien.de).

Zur Plattform AWMF:

In der AWMF (Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften e.V.) sind 175 wissenschaftliche Fachgesellschaften (+ 4 assoziierte) aus allen Bereichen der Medizin zusammengeschlossen. Die AWMF vertritt Deutschland im Council for International Organizations of Medical Sciences CIOMS. Die Website AWMF online soll Wissenschaftler im Bereich der Medizin und die breite Öffentlichkeit über alle Aktivitäten der AWMF informieren.

Andere Leitlinien sind mit entsprechendem Zugang im Internet (z.B. Link zu den Fachgesellschaften bzw. Verlagen) gekennzeichnet. Über deren Nutzungsbedingungen informieren die jeweiligen Homepages.

PubMed Central® (PMC): PMC is a free full-text archive of biomedical and life sciences journal literature at the U.S. National Institutes of Health's National Library of Medicine (NIH/NLM); (siehe: www.ncbi.nlm.nih.gov/pmc/). Über dieses Internetportal können Autoren Literatur frei zur Verfügung stellen, die dort auch als PDF-Datei zum Download zur Verfügung steht.

Nachtrag 2021:

Aufgrund der Anpassung von Leitlinien zum Thema Fettstoffwechsel hier die aktuellen Literaturstellen und Links:

Amerikanische Leitlinien

2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease: Executive Summary, A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines, *Circulation*. 2019; 140: e563–e595. DOI: 10.1161/CIR.0000000000000677.

<https://www.ahajournals.org/doi/10.1161/CIR.0000000000000678> und

[https://www.acc.org/clinical-topics/](https://www.acc.org/clinical-topics/dyslipidemia#sort=%40commonsortdate%20descending&tab=guidelines)

[dyslipidemia#sort=%40commonsortdate%20descending&tab=guidelines](https://www.acc.org/clinical-topics/dyslipidemia#sort=%40commonsortdate%20descending&tab=guidelines)

Europäische Leitlinien und deutsche Leitlinien

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk: The Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and European Atherosclerosis Society (EAS), *European Heart Journal* 2019; doi:10.1093/eurheartj/ehz455

<https://academic.oup.com/eurheartj/article/41/1/111/5556353?login=true>

(Stand 04.11.2021)

DGK-Pocket-Leitlinie Diagnostik und Therapie der Dyslipidämien (Version 2019)

Download <https://leitlinien.dgk.org/> und Online-Version

[https://www.amboss.com/de/wissen/DGK-Pocket-](https://www.amboss.com/de/wissen/DGK-Pocket-Leitlinie_Diagnostik_und_Therapie_der_Dyslipid%C3%A4mien_(Version_2019)/)

[Leitlinie_Diagnostik_und_Therapie_der_Dyslipid%C3%A4mien_\(Version_2019\)/](https://www.amboss.com/de/wissen/DGK-Pocket-Leitlinie_Diagnostik_und_Therapie_der_Dyslipid%C3%A4mien_(Version_2019)/)

(Stand 04.11.2021)

Diabetes und Fettstoffwechselstörung

Parhofer KG, Birkenfeld AL, Krone W, Lehrke M, Marx N, Merkel M, Schütt KS, Zirik A, Müller-Wieland D, Lipidtherapie bei Patienten mit Diabetes mellitus, *Diabetologie* 2020; 15 (Suppl 1): S160–S165. doi:10.1055/a-1193-3925.

<https://www.deutsche-diabetes-gesellschaft.de/behandlung/leitlinien>

(Stand 26.03.2021)

Leitlinie Risikoberatung kardiovaskuläre Prävention

Hausärztliche Risikoberatung zur kardiovaskulären Prävention S3-Leitlinie AWMF-Register-Nr. 053-024, DEGAM-Leitlinie Nr. 19 DEGAM 2017

Leitlinie Fettzufuhr und Prävention ernährungsbedingter Krankheiten

Evidenzbasierte Leitlinie: „Fettzufuhr und Prävention ausgewählter ernährungsmitbedingter Krankheiten“, 2. Version 2015,

<https://www.dge.de/wissenschaft/leitlinien/> und

<https://www.dge.de/wissenschaft/leitlinien/leitlinie-fett/?L=0>

Evidence-Based Guideline of the German Nutrition Society: Fat Intake and Prevention of Selected Nutrition-Related Diseases, *Ann Nutr Metab* 2015;67:141-204.

(DOI:10.1159/000437243) (Stand 04.11.2021)

Versorgungsleitlinie KHK

Nationale VersorgungsLeitlinie Chronische KHK, Stand: 01.04.2019 (in Überarbeitung), gültig bis 31.03.2024:

Langfassung, Kurzinformationen zu einzelnen Themenbereichen, Patientenleitlinie und Patienteninformationen in verschiedenen Sprachen

<https://www.awmf.org/leitlinien/detail/II/nvl-004.html>

Hyperlipidämien bei Kindern und Jugendlichen, Diagnostik und Therapie

Chourdakis M, Berthold Koletzko B im Auftrag der Arbeitsgemeinschaft für Pädiatrische Stoffwechselstörungen (APS) in der Deutschen Gesellschaft für Kinderheilkunde und Jugendmedizin e.V., S2k-Leitlinien zur Diagnostik und Therapie von Hyperlipidämien bei Kindern und Jugendlichen, AWMF-Register Nr.: 027-068, 15. April 2015.

<https://aps-med.de/leitlinien/>

(Stand 04.11.2021)

1 Einleitung

ESC/EAS Guidelines 2016:

Catapano AL, Graham I, Backer G, Wiklund O, Chapman MJ, Drexel H, Hoes AW, Jennings CS, Landmesser U, Pedersen TR et al, 2016 ESC/EAS Guidelines for the Management of Dyslipidaemias. Eur Heart J 2016; 37 (39): 2999-3058. DOI: <https://doi.org/10.1093/eurheartj/ehw272>. Published: 28 August 2016.

Siehe unter: <https://academic.oup.com/eurheartj/article/37/39/2999/2414995/2016-ESC-EAS-Guidelines-for-the-Management-of>.

Statistisches Bundesamt:

<https://www.destatis.de/DE/Startseite.html>

2 Kardiovaskuläres Risiko

ESC-HeartSCORE System:

<http://www.heartscore.org> (Stand 8.4.2017).

Die Tabellen, die HDL-C enthalten, auf der ESC-Webseite:

<http://www.escardio.org/guidelines>.

Mortalitätsdaten der WHO 2012:

<http://apps.who.int/gho/data/node.main.A865CARDIOVASCULAR?lang=en>

2.1 Risikokategorien

Europäische und nordamerikanische Leitlinien:

ESC/EAS Guidelines 2016:

2016 ESC/EAS Guidelines for the Management of Dyslipidaemias. Eur Heart J 2016; 37; 3014-3019 (2999–3058), doi:10.1093/eurheartj/ehw272.

<https://academic.oup.com/eurheartj/article/37/39/2999/2414995/2016-ESC-EAS-Guidelines-for-the-Management-of>, siehe auch unter: <https://leitlinien.dgk.org/2016/2016-esceas-guidelines-for-the-management-of-dyslipidaemias/>.

AACE 2017 Guidelines:

Jellinger PS et al, American Association of Clinical Endocrinologists and American College of Endocrinology Guidelines for Management of Dyslipidemia and Prevention of Cardiovascular Disease. Endocr Pract. 2017 Feb 3, Rapid Electronic Article in Press, DOI:10.4158/EP171764.GL; © 2017 AACE.

Siehe unter <https://www.aace.com/article/129> oder <https://www.aace.com/files/lipid-guidelines.pdf>.

ESC-HeartSCORE System:

<http://www.heartscore.org>.

Cooney MT, Dudina AL, Graham IM. Value and limitations of existing scores for the assessment of cardiovascular risk: a review for clinicians. *J Am Coll Cardiol* 2009; 54:1209–1227.

Cooney MT, Dudina A, D'Agostino R, Graham IM. Cardiovascular risk-estimation systems in primary prevention: do they differ? Do they make a difference? Can we see the future? *Circulation* 2010;122:300–310.

Lloyd-Jones DM, Leip EP, Larson MG, D'Agostino RB, Beiser A, Wilson PW, Wolf PA, Levy D. Prediction of lifetime risk for cardiovascular disease by risk factor burden at 50 years of age. *Circulation* 2006;113:791–798.

Cooney MT, Selmer R, Lindman A, Tverdal A, Menotti A, Thomsen T, DeBacker G, De Bacquer D, Tell GS, Njolstad I, Graham IM. Cardiovascular risk estimation in older persons: SCORE O.P. *Eur J Prev Cardiol* 2016;23:1093–1103.

Cooney MT, Dudina A, De Bacquer D, Wilhelmsen L, Sans S, Menotti A, De Backer G, Jousilahti P, Keil U, Thomsen T, Whincup P, Graham IM. HDL cholesterol protects against cardiovascular disease in both genders, at all ages and at all levels of risk. *Atherosclerosis* 2009;206:611–616.

Cooney MT, Dudina A, De Bacquer D, Fitzgerald A, Conroy R, Sans S, Menotti A, De Backer G, Jousilahti P, Keil U, Thomsen T, Whincup P, Graham I. How much does HDL cholesterol add to risk estimation? A report from the SCORE Investigators. *Eur J Cardiovasc Prev Rehabil* 2009;16:304–314.

Mortensen MB, Afzal S, Nordestgaard BG, Falk E. The high-density lipoprotein-adjusted SCORE model worsens SCORE-based risk classification in a contemporary population of 30,824 Europeans: the Copenhagen General Population Study. *Eur Heart J* 2015;36:2446–2453.

Kavousi M, Elias-Smale S, Rutten JH, Leening MJ, Vliegenthart R, Verwoert GC, Krestin GP, Oudkerk M, de Maat MP, Leebeek FW, Mattace-Raso FU, Lindemans J, Hofman A, Steyerberg EW, van der Lugt A, van den Meiracker AH, Witteman JC. Evaluation of newer risk markers for coronary heart disease risk classification: a cohort study. *Ann Intern Med* 2012;156:438–444.

Yeboah J, McClelland RL, Polonsky TS, Burke GL, Sibley CT, O'Leary D, Carr JJ, Goff DC, Greenland P, Herrington DM. Comparison of novel risk markers for improvement in cardiovascular risk assessment in intermediate-risk individuals. *JAMA* 2012;308:788–795.

Vlachopoulos C, Xaplanteris P, Aboyans V, Brodmann M, Cifkova R, Cosentino F, De Carlo M, Gallino A, Landmesser U, Laurent S, Lekakis J, Mikhailidis DP, Naka KK, Protogerou AD, Rizzoni D, Schmidt-Trucksäss A, Van Bortel L, Weber T, Yamashina A, Zimlichman R, Boutouyrie P, Cockcroft J, O'Rourke M, Park JB, Schillaci G, Sillesen H, Townsend RR. The role of vascular biomarkers for primary and secondary prevention. A position paper from the European Society of Cardiology Working Group on peripheral

circulation: endorsed by the Association for Research into Arterial Structure and Physiology (ARTERY) Society. *Atherosclerosis* 2015;241:507–532.

2.2 Nordamerikanische Leitlinien und Risikokalkulation

Nordamerikanische Leitlinien 2013:

Stone NJ, Robinson JG, Lichtenstein AH, C. Merz CNB, Blum CB, Eckel RH, Goldberg AC, Gordon D, Levy D, Lloyd-Jones DM, 2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults, *JACC (Journal of the American College of Cardiology)* 2014; 63 (Issue 25, Part B): 2889-2934; <https://doi.org/10.1016/j.jacc.2013.11.002>.

Download unter: <http://linkinghub.elsevier.com/retrieve/pii/S0735109713060282> oder http://www.onlinejacc.org/content/accj/63/25_Part_B/2889.full.pdf?_ga=2.68930897.1927809977.1507995955-781474009.1507995955 bzw. <http://www.acc.org/latest-in-cardiology/articles/2016/01/26/13/52/the-2015-acc-aha-focused-update-of-secondary-prevention-lipid-performance-measures>

Updates zu den Nordamerikanischen Leitlinien 2016:

Download unter:

http://www.onlinejacc.org/content/accj/63/25_Part_B/2889.full.pdf?_ga=2.68930897.1927809977.1507995955-781474009.1507995955,
<http://www.acc.org/latest-in-cardiology/articles/2016/01/26/13/52/the-2015-acc-aha-focused-update-of-secondary-prevention-lipid-performance-measures>
und
http://www.acc.org/guidelines#first=10&sort=%40foriginalz32xpostedz32xdate86069%20descending&f:@fdocumentz32xtype86069_76ad5b9d634f4299bcd73cedf2dbbb99=%5BGuidelines

AACE 2017 Guidelines:

Jellinger PS et al, American Association of Clinical Endocrinologists and American College of Endocrinology Guidelines for Management of Dyslipidemia and Prevention of Cardiovascular Disease. *Endocr Pract.* 2017 Feb 3, Rapid Electronic Article in Press, DOI:10.4158/EP171764.GL; © 2017 AACE.

<https://www.aace.com/article/129> oder <https://www.aace.com/files/lipid-guidelines.pdf>.

Final Recommendation Statement: Statin Use for the Primary Prevention of Cardiovascular Disease in Adults: Preventive Medication. U.S. Preventive Services Task Force. November 2016. <https://www.uspreventiveservicestaskforce.org/Page/Document/RecommendationStatementFinal/statin-use-in-adults-preventive-medication1>.

Pooled Cohort Risk Assessment Equations:

<http://clincalc.com/cardiology/ascvd/PooledCohort.aspx>.

Boekholdt SM, Hovingh GK, Mora S, Arsenault BJ, Amarenco P, Pedersen TR, LaRosa JC, Waters DD, DeMicco DA, Simes RJ, Keech AC, Colquhoun D, Hitman GA, Betteridge DJ, Clearfield MB, Downs JR, Colhoun HM, Gotto AM Jr, Ridker PM, Grundy SM, Kastelein JJ, Very low levels of atherogenic lipoproteins and the risk for cardiovascular events: a meta-analysis of statin trials, *J Am Coll Cardiol* 2014; 64: 485–494.

Brugts JJ, Yetgin T, Hoeks SE, Gotto AM, Shepherd J, Westendorp RG, de Craen AJ, Knopp RH, Nakamura H, Ridker P, van Domburg R, Deckers JW, The benefits of statins in people without established cardiovascular disease but with cardiovascular risk factors: meta-analysis of randomised controlled trials, *BMJ* 2009; 338: b2376.

Cannon CP, Blazing MA, Giugliano RP, McCagg A, White JA, Theroux P, Darius H, Lewis BS, Ophuis TO, Jukema JW, De Ferrari GM, Ruzylo W, De Lucca P, Im K, Bohula EA, Reist C, Wiviott SD, Tershakovec AM, Musliner TA, Braunwald E, Califf RM, Ezetimibe added to statin therapy after acute coronary syndromes, *N Engl J Med* 2015; 372: 2387–2397.

Cholesterol Treatment Trialists' (CTT) Collaboration, Baigent C, Blackwell L, Emberson J, Holland LE, Reith C, Bhalra N, Peto R, Barnes EH, Keech A, Simes J, Collins R, Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170,000 participants in 26 randomised trials, *Lancet* 2010; 376: 1670–1681.

Cholesterol Treatment Trialists' (CTT) Collaboration, Fulcher J, O'Connell R, Voysey M, Emberson J, Blackwell L, Mihaylova B, Simes J, Collins R, Kirby A, Colhoun H, Braunwald E, La Rosa J, Pedersen TR, Tonkin A, Davis B, Sleight P, Franzosi MG, Baigent C, Keech A, Efficacy and safety of LDL-lowering therapy among men and women: meta-analysis of individual data from 174,000 participants in 27 randomised trials, *Lancet* 2015; 385: 1397–1405.

Cholesterol Treatment Trialists' (CTT) Collaborators, Mihaylova B, Emberson J, Blackwell L, Keech A, Simes J, Barnes EH, Voysey M, Gray A, Collins R, Baigent C, The effects of lowering LDL cholesterol with statin therapy in people at low risk of vascular disease: meta-analysis of individual data from 27 randomised trials, *Lancet* 2012; 380: 581–590.

Hegele RA, Ginsberg HN, Chapman MJ, Nordestgaard BG, Kuivenhoven JA, Averna M, Bore'n J, Bruckert E, Catapano AL, Descamps OS, Hovingh GK, Humphries SE, Kovanen PT, Masana L, Pajukanta P, Parhofer KG, Raal FJ, Ray KK, Santos RD, Stalenhoef AF, Stroes E, Taskinen MR, Tybjaerg-Hansen A, Watts GF, Wiklund O, The polygenic nature of hypertriglyceridaemia: implications for definition, diagnosis and management, *Lancet Diabetes Endocrinol* 2014; 2: 655–666.

Mills EJ, Rachlis B, Wu P, Devereaux PJ, Arora P, Perri D. Primary prevention of cardiovascular mortality and events with statin treatments: a network meta-analysis involving more than 65,000 patients, *J Am Coll Cardiol* 2008; 52: 1769–1781.

Pedersen TR, Faergeman O, Kastelein JJ, Olsson AG, Tikkanen MJ, Holme I, Larsen ML, Bendixen FS, Lindahl C, Szarek M, Tsai J. High-dose atorvastatin vs usual-dose simvastatin for secondary prevention after myocardial infarction: the IDEAL study: a randomized controlled trial, *JAMA* 2005; 294: 2437–2445.

SPRINT Research Group, Wright JT Jr, Williamson JD, Whelton PK, Snyder JK, Sink KM, Rocco MV, Reboussin DM, Rahman M, Oparil S, Lewis CE, Kimmel PL, Johnson KC, Goff DC Jr, Fine LJ, Cutler JA, Cushman WC, Cheung AK, Ambrosius WT. A randomized trial of intensive versus standard blood-pressure control, *N Engl J Med* 2015; 373: 2103–2116.

Stone NJ, Robinson JG, Lichtenstein AH, Bairey Merz CN, Blum CB, Eckel RH, Goldberg AC, Gordon D, Levy D, Lloyd-Jones DM, McBride P, Schwartz JS, Shero ST, Smith SC Jr, Watson K, Wilson PW, Eddleman KM, Jarrett NM, LaBresh K, Nevo L, Wnek J, Anderson JL, Halperin JL, Albert NM, Bozkurt B, Brindis RG, Curtis LH, DeMets D, Hochman JS, Kovacs RJ, Ohman EM, Pressler SJ, Sellke FW, Shen WK, Smith SC Jr, Tomaselli GF, 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardio-vascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines, *Circulation* 2014; 129(25 Suppl 2): S1–S45.

2.3 Empfehlungen der Bundesärztekammer

siehe Leitlinien und:

Therapieempfehlungen der Arzneimittelkommission der deutschen Ärzteschaft
Fettstoffwechselstörungen – 3. Auflage 2012; Download unter:
[https://www.akdae.de/Arzneimitteltherapie/TE/A-Z/PDF/
Fettstoffwechselstoerungen.pdf#page=1&view=fitB](https://www.akdae.de/Arzneimitteltherapie/TE/A-Z/PDF/Fettstoffwechselstoerungen.pdf#page=1&view=fitB)

Framingham risk score:

D’Agostino RB Sr, Vasan RS, Pencina MJ, Wolf PA, Cobain M, Massaro JM, Kannel WB. General cardiovascular risk profile for use in primary care: the Framingham Heart Study, *Circulation* 2008; 117: 743–753.

PROCAM Algorithmus:

Assmann G, Cullen P, Schulte H. Simple scoring scheme for calculating the risk of acute coronary events based on the 10-year follow-up of the prospective cardiovascular Munster (PROCAM) study, *Circulation* 2002; 105: 310–315.

ESC-HeartSCORE:

Conroy RM, Pyorala K, Fitzgerald AP, Sans S, Menotti A, De Backer G, De Bacquer D, Ducimetie`re P, Jousilahti P, Keil U, Njølstad I, Oganov RG, Thomsen T, Tunstall-Pedoe H, Tverdal A, Wedel H, Whincup P, Wilhelmsen L, Graham IM. Estimation of ten-year risk of fatal cardiovascular disease in Europe: the SCORE project, *Eur Heart J* 2003; 24: 987–1003.

ARRIBA:

<https://www.arriba-hausarzt.de>

3 Laborparameter

3.1 Screening

Kolovou GD, Mikhailidis DP, Kovar J, Lairon D, Nordestgaard BG, Ooi TC, Perez-Martinez P, Bilianou H, Anagnostopoulou K, Panotopoulos G. Assessment and clinical relevance of non-fasting and postprandial triglycerides: an expert panel statement, *Curr Vasc Pharmacol* 2011; 9: 258–270.

Mihas C, Kolovou GD, Mikhailidis DP, Kovar J, Lairon D, Nordestgaard BG, Ooi TC, Perez-Martinez P, Bilianou H, Anagnostopoulou K, Panotopoulos G. Diagnostic value of postprandial triglyceride testing in healthy subjects: a meta-analysis, *Curr Vasc Pharmacol* 2011; 9: 271–280.

Nordestgaard BG, Varbo A. Triglycerides and cardiovascular disease, *Lancet* 2014; 384: 626–635.

Jorgensen AB, Frikke-Schmidt R, West AS, Grande P, Nordestgaard BG, Tybjaerg-Hansen A. Genetically elevated non-fasting triglycerides and calculated remnant cholesterol as causal risk factors for myocardial infarction, *Eur Heart J* 2013; 34: 1826–1833.

Langsted A, Nordestgaard BG. Nonfasting lipids, lipoproteins, and apolipoproteins in individuals with and without diabetes: 58 434 individuals from the Copenhagen General Population Study, *Clin Chem* 2011; 57: 482–489.

3.2 Lipoproteine

Rabar S, Harker M, O'Flynn N, Wierzbicki AS, Guideline Development Group, Lipid modification and cardiovascular risk assessment for the primary and secondary prevention of cardiovascular disease: summary of updated NICE guidance, *BMJ* 2014; 349: g4356.

3.3 Gesamtcholesterin (TC)

Joint British Societies' consensus recommendations for the prevention of cardiovascular disease (JBS3), *Heart* 2014; 100(Suppl 2): ii1–ii67.

3.4 LDL-C

Knopfholz J, Disserol CC, Pierin AJ, Schirr FL, Streisky L, Takito LL, Massucheto Ledesma P, Faria-Neto JR, Olandoski M, da Cunha CL, Bandeira AM, Validation of the Friedewald formula in patients with metabolic syndrome, *Cholesterol* 2014; 2014: 261878. <https://www.ncbi.nlm.nih.gov/pubmed/24672715> .

National Institute for Health and Care Excellence, Lipid modification: cardiovascular risk assessment and the modification of blood lipids for the primary and secondary prevention

of cardiovascular disease, London: National Institute for Health and Care Excellence, 2014. <https://www.ncbi.nlm.nih.gov/pubmed/25340243> .

3.5 HDL-C

Di Angelantonio E, Sarwar N, Perry P, Kaptoge S, Ray KK, Thompson A, Wood AM, Lewington S, Sattar N, Packard CJ, Collins R, Thompson SG, Danesh J, Major lipids, apolipoproteins, and risk of vascular disease, *JAMA* 2009; 302: 1993–2000.

Khera AV, Cuchel M, de la Llera-Moya M, Rodrigues A, Burke MF, Jafri K, French BC, Phillips JA, Mucksavage ML, Wilensky RL, Mohler ER, Rothblat GH, Rader DJ, Cholesterol efflux capacity, high-density lipoprotein function, and atherosclerosis, *N Engl J Med* 2011; 364: 127–135.

Li XM, Tang WH, Mosior MK, Huang Y, Wu Y, Matter W, Gao V, Schmitt D, Didonato JA, Fisher EA, Smith JD, Hazen SL, Paradoxical association of enhanced cholesterol efflux with increased incident cardiovascular risks, *Arterioscler Thromb Vasc Biol* 2013; 33: 1696–1705.

Rohatgi A, Khera A, Berry JD, Givens EG, Ayers CR, Wedin KE, Neeland IJ, Yuhanna IS, Rader DR, de Lemos JA, Shaul PW, HDL cholesterol efflux capacity and incident cardiovascular events, *N Engl J Med* 2014; 371: 2383–2393.

Delalla OF, Elliott HA, Gofman JW, Ultracentrifugal studies of high density serum lipoproteins in clinically healthy adults, *Am J Physiol* 1954; 179(2): 333-7.

3.6 Triglyceride (TG)

Sarwar N, Danesh J, Eiriksdottir G, Sigurdsson G, Wareham N, Bingham S, Boekholdt SM, Khaw KT, Gudnason V, Triglycerides and the risk of coronary heart disease: 10,158 incident cases among 262,525 participants in 29 Western prospective studies, *Circulation* 2007; 115: 450–458.

Hokanson JE, Austin MA, Plasma triglyceride level is a risk factor for cardiovascular disease independent of high-density lipoprotein cholesterol level: a meta-analysis of population-based prospective studies, *J Cardiovasc Risk* 1996; 3: 213–219.

Jorgensen AB, Frikke-Schmidt R, West AS, Grande P, Nordestgaard BG, Tybjaerg-Hansen A, Genetically elevated non-fasting triglycerides and calculated remnant cholesterol as causal risk factors for myocardial infarction, *Eur Heart J* 2013; 34: 1826–1833.

3.7 Apolipoproteine

Charlton-Menys V, Betteridge DJ, Colhoun H, Fuller J, France M, Hitman GA, Livingstone SJ, Neil HA, Newman CB, Szarek M, DeMicco DA, Durrington PN, Targets of statin therapy: LDL cholesterol, non-HDL cholesterol, and apolipoprotein B in type 2

diabetes in the Collaborative Atorvastatin Diabetes Study (CARDS), Clin Chem 2009; 55: 473–480.

Taskinen MR, Barter PJ, Ehnholm C, Sullivan DR, Mann K, Simes J, Best JD, Hamwood S, Keech AC, Ability of traditional lipid ratios and apolipoprotein ratios to predict cardiovascular risk in people with type 2 diabetes, Diabetologia 2010; 53: 1846–1855.

Sniderman AD, Williams K, Contois JH, Monroe HM, McQueen MJ, de Graaf J, Furberg CD, A meta-analysis of low-density lipoprotein cholesterol, non-high-density lipoprotein cholesterol, and apolipoprotein B as markers of cardiovascular risk, Circ Cardiovasc Qual Outcomes 2011; 4: 337–345.

Onat A, Hergenc G, Sansoy V, Fobker M, Ceyhan K, Toprak S, Assmann G, Apolipoprotein C-III, a strong discriminant of coronary risk in men and a determinant of the metabolic syndrome in both genders, Atherosclerosis 2003; 168: 81–89.

Sacks FM, Alaupovic P, Moya LA, Cole TG, Sussex B, Stampfer MJ, Pfeffer MA, Braunwald E, VLDL, apolipoproteins B, CIII, and E, and risk of recurrent coronary events in the Cholesterol and Recurrent Events (CARE) trial, Circulation 2000; 102: 1886–1892.

Jorgensen AB, Frikke-Schmidt R, Nordestgaard BG, Tybjaerg-Hansen A, Loss-of-function mutations in APOC3 and risk of ischemic vascular disease, N Engl J Med 2014; 371: 32–41.

3.8 Lipoprotein (a) (Lp(a))

Lp(a): Kausaler Risikofaktor für koronare Herzkrankheit

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4.5 Empfehlungen

4.5.1 Keine Diäten

4.5.2 Immer satt sein

4.5.3 Keine flüssigen Kalorien

4.5.4 Abends keine Kohlenhydrate - auch kein Obst

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4.5.11 Phytosterine

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5 Therapie der Fettstoffwechselstörung

5.1 Medikamentöse Therapie

5.1.1 Statine

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9.3.5 Basisbehandlung der Hypertonie

Lebensstilveränderungen:

Empfehlungen der Leitlinie 2014, Pocket-Leitlinien Arterielle Hypertonie:

ESC Pocket Guidelines, Leitlinien für das Management der arteriellen Hypertonie, Hrgs. Deutsche Gesellschaft für Kardiologie e.V. und Deutsche Hochdruckliga e.V., Verlag B. Bruckmeier GmbH 2013, ISBN 978-3-89862-948-5, 46 Seiten.

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9.3.6 Medikamentöse Therapie

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9.4 Diabetes mellitus und metabolisches Syndrom

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<http://www.diabetesatlas.org/>.

Auswertung auf Basis bundesweiter vertragsärztlicher Abrechnungsdaten:

Goffrier B, Schulz M, Bätzing-Feigenbaum J. Administrative Prävalenzen und Inzidenzen des Diabetes mellitus von 2009 bis 2015. Zentralinstitut für die kassenärztliche Versorgung in Deutschland (Zi). Versorgungsatlas-Bericht Nr. 17/03. Berlin 2017. DOI: 10.20364/VA-17.03. URL: <http://www.versorgungsatlas.de/themen/alle-analysen-nach-datum-sortiert/?tab=6&uid=79>.

Deutscher Gesundheitsbericht Diabetes 2016:

https://www.diabetesde.org/system/files/documents/fileadmin/users/Patientenseite/PDFs_und_TEXTE/Infomaterial/Gesundheitsbericht_2016.pdf

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https://www.diabetesde.org/system/files/documents/gesundheitsbericht_2017.pdf

9.4.1 Diabetestypen

WHO 1999, Definition, Diagnosis and Classification of Diabetes Mellitus and its Complications: http://apps.who.int/iris/bitstream/10665/66040/1/WHO_NCD_NCS_99.2.pdf

9.4.2 Genetische Veranlagung zum Diabetes mellitus Typ 2

Genforschung zu Diabetes:

Diabetesinformationsdienst München / Helmholtz-Zentrum München;
<https://www.diabetesinformationsdienst-muenchen.de/forschung/genforschung/index.html>

Evidenzbasierte Leitlinie / Nationale Versorgungsleitlinie Therapie des Typ-2-Diabetes, 1. Aufl. Version 4, Stand November 2014, Seiten 69-74; http://www.deutsche-diabetes-gesellschaft.de/fileadmin/Redakteur/Leitlinien/Evidenzbasierte_Leitlinien/NVL_Therapie_DM2_lang_Aug_13_geae_Nov_2014.pdf

9.4.3 Wie entsteht ein Diabetes mellitus Typ 2?

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Ferrannini E, DeFronzo RA, Impact of glucose-lowering drugs on cardiovascular disease in type 2 diabetes, *Eur Heart J* 2015 Sep 7; 36(34): 2288-96. doi: 10.1093/eurheartj/ehv239. Epub 2015 Jun 10.

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ACCORD Study Group, Gerstein HC, Miller ME, Genuth S, Ismail-Beigi F, Buse JB, Goff DC Jr, Probstfield JL, Cushman WC, Ginsberg HN, Bigger JT, Grimm RH Jr, Byington RP, Rosenberg YD, Friedewald WT, Long-term effects of intensive glucose lowering on cardiovascular outcomes, *N Engl J Med* 2011 Mar 3; 364(9): 818-28. doi: 10.1056/NEJMoa1006524.

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9.4.5 Metabolisches Syndrom

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Mensink GBM, Schienkiewitz A, Haftenberger M, Lampert T, Ziese T, Scheidt-Nave C, Übergewicht und Adipositas in Deutschland, Ergebnisse der Studie zur Gesundheit Erwachsener in Deutschland (DEGS1), Bundesgesundheitsbl 2013; 56: 786–794; DOI 10.1007/s00103-012-1656-3; Springer-Verlag Berlin Heidelberg 2013.

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Übergewicht und Adipositas von Männern und Frauen in Deutschland und USA:

Mensink GBM et al, DEGS-Symposium (Robert Koch Institut) 2012 - Studie zur Gesundheit Erwachsener in Deutschland, Übergewicht und Adipositas in Deutschland: Werden wir immer dicker?, Factsheets und Tabellen; siehe unter:

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KDIGO Board Members, Kidney Disease, Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease, Kidney Inter Suppl. 2013; 3(1): 1-150. http://www.kdigo.org/clinical_practice_guidelines/pdf/CKD/KDIGO_2012_CKD_GL.pdf.

10 Risikomarker

10.1 C-reaktives Protein

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10.2 Atherosklerose als inflammatorischer Prozess

Koenig W, Hoffmeister A, Khuseyinova N, Imhof A, Atherosklerose als inflammatorischer Prozess: C-reaktives Protein und koronares Risiko, *Dtsch Arztebl* 2003; 100(3): A 117–126, B 108, C105.

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10.3 Ist CRP ein kausaler Faktor für kardiovaskuläre Erkrankungen?

Zellkulturmodelle fördern CRP Faktoren der endothelialen Dysfunktion und Plaquentstehung:

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Venugopal SK, Devaraj S, Yuhanna I, Shaul P, Jialal I Demonstration that C-reactive protein decreases eNOS expression and bioactivity in human aortic endothelial cells, *Circulation* 2002; 106(12): 1439-41.

Hyperlipidämie und Atherosklerose bei CRP-transgenen Mäusen:

Paul A, Ko KW, Li L, Yechoor V, McCrory MA, Szalai AJ et al, C-reactive protein accelerates the progression of atherosclerosis in apolipoprotein E-deficient mice, *Circulation* 2004; 109(5): 647-55. doi:10.1161/01.CIR.0000114526.50618.24.

CRP-Präparationen mit bakteriellen Lipopolysacchariden verunreinigt:

Nerurkar SS, McDevitt PJ, Scott GF, Johanson KO, Willette RN, Yue TL, Lipopolysaccharide (LPS) contamination plays the real role in C-reactive protein-induced IL-6 secretion from human endothelial cells in vitro, *Arterioscler Thromb Vasc Biol* 2005; 25(9): e136.

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Ridker PM, High-sensitivity C-reactive protein, inflammation and cardiovascular risk: from concept to clinical practice to clinical benefit, *Am Heart J* 2004; 148(1 Suppl): S19-26. doi:10.1016/j.ahj.2004.04.028.

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<http://whs.bwh.harvard.edu/>
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Ridker PM, Cannon CP, Morrow D, Rifai N, Rose LM, McCabe CH et al, C-reactive protein levels and outcomes after statin therapy, *N Engl J Med* 2005; 352(1): 20-8. doi:10.1056/NEJMoa042378.

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März W, Winkler K, Nauck M, Boehm BO, Winkelmann BR, Effects of statins on C-reactive protein and interleukin-6 (the Ludwigshafen Risk and Cardiovascular Health study), *Am J Cardiol* 2003; 92(3): 305-8.

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Arnaud C, Burger F, Steffens S, Veillard NR, Nguyen TH, Trono D et al, Statins reduce interleukin-6-induced C-reactive protein in human hepatocytes: new evidence for direct antiinflammatory effects of statins, *Arterioscler Thromb Vasc Biol* 2005; 25(6): 1231-6. doi:10.1161/01.ATV.0000163840.63685.0c.

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Chasman DI, Kozlowski P, Zee RY, Kwiatkowski DJ, Ridker PM, Qualitative and quantitative effects of APOE genetic variation on plasma C-reactive protein, LDL-cholesterol, and apoE protein, *Genes Immun* 2006; 7(3): 211-9. doi:10.1038/sj.gene.6364289.

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10.5 Ist Homozystein ein kausaler Biomarker für KHK?

10.5.1 Homozystein und Atherosklerose

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Malinow MR, Bostom AG, Krauss RM, Homocyst(e)ine, diet, and cardiovascular diseases: a statement for healthcare professionals from the Nutrition Committee, American Heart Association, *Circulation* 1999; 99(1): 178-82.

Homozystinurie:

McCully KS, Vascular pathology of homocysteinemia: implications for the pathogenesis of arteriosclerosis, *Am J Pathol* 1969; 56(1): 111-28.

Endotheliale Dysfunktion:

Bellamy MF, McDowell IF, Ramsey MW, Brownlee M, Bones C, Newcombe RG et al, Hyperhomocysteinemia after an oral methionine load acutely impairs endothelial function in healthy adults, *Circulation* 1998; 98(18): 1848-52.

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Eberhardt RT, Forgione MA, Cap A, Leopold JA, Rudd MA, Trolliet M et al, Endothelial dysfunction in a murine model of mild hyperhomocyst(e)inemia, J Clin Invest 2000; 106(4): 483-91. doi:10.1172/JCI8342.

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Zhou J, Werstuck GH, Lhotak S, de Koning AB, Sood SK, Hossain GS et al, Association of multiple cellular stress pathways with accelerated atherosclerosis in hyperhomocysteinemic apolipoprotein E-deficient mice, Circulation 2004; 110(2): 207-13. doi:10.1161/01.CIR.0000134487.51510.97.

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Wald DS, Law M, Morris JKI, Homocysteine and cardiovascular disease: evidence on causality from a meta-analysis, BMJ 2002; 325(7374): 1202.

10.5.3 Interventionsstudien mit Vitaminsubstitution*Vitaminsubstitution vermindert nicht Risiko kardiovaskulärer Ereignisse oder Tod:*

Bazzano LA, Reynolds K, Holder KN, He J, Effect of folic acid supplementation on risk of cardiovascular diseases: a meta-analysis of randomized controlled trials, JAMA 2006; 296(22): 2720-6. doi:10.1001/jama.296.22.2720.

Vitamin Intervention for Stroke Prevention (VISP)-Studie:

Toole JF, Malinow MR, Chambless LE, Spence JD, Pettigrew LC, Howard VJ et al, Lowering homocysteine in patients with ischemic stroke to prevent recurrent stroke, myocardial infarction, and death: the Vitamin Intervention for Stroke Prevention (VISP) randomized controlled trial, JAMA. 2004; 291(5): 565-75. doi:10.1001/jama.291.5.565.

Norwegian Vitamin (NORVIT)-Studie:

Bonaa KH, Njolstad I, Ueland PM, Schirmer H, Tverdal A, Steigen T et al, Homocysteine lowering and cardiovascular events after acute myocardial infarction, *N Engl J Med* 2006; 354(15): 1578-88. doi:10.1056/NEJMoa055227.

HOPE-2-Studie:

Lonn E, Yusuf S, Arnold MJ, Sheridan P, Pogue J, Micks M, McQueen MJ, Probstfield J, Fodor G, Held C, Genest J Jr, The Heart Outcomes Prevention Evaluation (HOPE) 2 Investigators, Homocysteine lowering with folic acid and B vitamins in vascular disease, *N Engl J Med* 2006 Apr 13; 354(15): 1567-77. Epub 2006 Mar 12.

Women's Antioxidant and Folic Acid Cardiovascular Study (WAFACS) (American Heart Association 2006):

Albert CM, M.P.H. Cook NR, Gaziano JM, Zaharris E, MacFadyen J, Danielson E, Buring JE, Manson JE, Effect of Folic Acid and B-Vitamins on Risk of Cardiovascular Events and Total Mortality among Women at High Risk for Cardiovascular Disease: A Randomized Trial, *JAMA* 2008 May 7; 299(17): 2027–2036.

Western Norway B-vitamin Intervention Trial (WENBIT):

Løland KH, Bleie O, Blix AJ, Strand E, Ueland PM, Refsum H, Ebbing M, Nordrehaug JE, Nygård O, Effect of homocysteine-lowering B vitamin treatment on angiographic progression of coronary artery disease: a Western Norway B Vitamin Intervention Trial (WENBIT) substudy, *Am J Cardiol* 2010 Jun 1; 105(11): 1577-84. doi: 10.1016/j.amjcard.2010.01.019. Epub 2010 Apr 10.

10.5.4 Das Dilemma der Homozysteinstudien

Versagen der Vitaminsubstitution:

Kaul S, Zadeh AA, Shah PK, Homocysteine hypothesis for atherothrombotic cardiovascular disease: not validated, *J Am Coll Cardiol* 2006; 48: 914-23. Epub 2006 Aug 17.

Liem A, Reynierse-Buitenwerf GH, Zwinderman AH, Jukema JW, van Veldhuisen DJ, Secondary prevention with folic acid: effects on clinical outcomes, *J Am Coll Cardiol* 2003; 41(12): 2105-13.

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10.5.5 Homozystein und KHK – eine Schlußfolgerung

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