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Introduction

Kp'3; ; : .'Eqpi tguu'uwr r qtvgf 'ý g'þggf 'hqt'dcuke''cpf ''enkplecntgugctej 'kp'Eqtqpct { 'Ctvgt { ''cpf '' Rtquvcvg''F kugcug'kp'qtf gt''q'tgf weg''y g'kpekf gpeg''qh'y gug'htlg/ y tgcvgpkpi 'f kugcugu'cpf 'f gxgmr '' o qtg''ghtgevkxg.''o qtg''ur gektle.''cpf ''guu'kpxcukxg'hqto u''qh'y gtcr { 'hqt'r cvkgpwl'*Rvdrke''Ncy 'P q0' 327/484+0Kp'H[32.''y g'Kpvgi tcvkxg'Ectf kce'J gcnj 'Rtqlgev*KEJ R+'y cu'kf gpvkhgf ''cu'c'' ectf kqxcuewrct'*EX+''tgugctej 'Egpvgt''qh'Gzegngpeg'*EQG+''d{ 'J gcnj 'Chicktu''cpf 'r megf 'kpvq''y g'' Cto { 'Rtqi tco 'Qdlgevkxg''O go qtcpf wo '*RQO +0KEJ R'eqpvkpvgu'kwu'qr gtcvkqp''cv'y g'Y cngt 'Tggf '' P cvkqpcn'O ktkxt{ ''O gf kecn'Egpvgt''*Y TP O O E+'kp'Dgy guf c.'O ct { mpf 0'

Ectf kaxcuewet "F kugcug"*EXF +tkuniku"cv'gr kf go ke'r tqr qt kqpu'kp'y g'O ktket { "J genj 'U{ugo " *O J U+0J getv'f kugcug'ku'y g'o quv'eqo o qp. 'equvn{. 'cpf 'r tgxgpvcdmg'qh'em'j genj 'r tqdrgo u'epf 'y g'' O J U'j cu'e 'reti g'pwo dgt'qh'dgpghkeketkgu'ev'tkunihqt 'EXF 0Ectf kee'tgrevgf 'gxgpvu'o eng'wr 'e'' uki pkheepv'r qtvkqp''qh'pqp/dcwrg'f kugcug'kplwtkgu'tgs wktkpi ''gxcewevkqp'htqo ''Vj gevgt''lgqr etf k kpi " qr gtevkqpen'ghtgevkxgpguu0Ugtxkeg'o go dgtu'y kj 'o wnkr rg'eqo dev'f gr m{o gpvu'epf 'Y qwpf gf '' Y ettkqtu'j exg'kpetgeugf 'EXF 'o qtdkf ks{ lo qtverks{ "tkuni*4"epf '507'hqrf. 'tgur gevkxgn{+0^{3.4}'F gur kg'' qr vko en'o gf keen'y gter { 'uwej 'ecu'uvevkpu 'y gtg'tgo ekpu'e' 'tgukf wen'EXF 'tkuniqh'er r tqzko evgn{ '' 8; ' 0⁵'Gzkuvkpi 'y gmpguu'r tqi teo u'kp'y g'F gr etvo gpv'qh'F ghepug'*F QF +'epf 'ekxtkep' j genj eetg'' f q'pqv'ef gs wevgn{ ''eff tguu'EXF 'tkuniqt''qduveengu'tgrevgf ''q'j genj { ''hxkpi ''y j kj ''epqxevkxg. ''kpegukxg.'' o wnk'o gej epkuvke'er r tqeej gu'q'kor tqxg'EXF ''qweqo gu0Vj gtg'ku'e'etkkeenipggf 'hqt'' r gtuqperk{ gf 'EXF 'tkunitgf wevkqp''epf ''eevkqpedrg''go r qy gto gpv'uvtevgi kgukqqnu'vq''qr vko k{ g'j genj '' epf 'tgf weg''equv0'''

Vj g'KEJ R'*J IH+'ej co r kqpu'ý g'y c{'hqt'qr vko cn'EX'J gcnj 'kp'ý g'OJ U'd{'eqpf wevkpi "pqxgn' tgugctej 'wkhk kpi 'c'U{urgo u'Dkqni { lr gtuqpcnk gf 'o gf kekpg'f guki p'vq'f kueqxgt'cpf 'f gxgnr " r tcevkecn'r tg/go r vkxg''cpf 'kpygi tcvkxg''cr r tqcej gu'kp''qtf gt''q'f gygev'cpf 'eqo dcv'EXF 'gctnkgt''cpf " cwi o gpv'vtcf kkqpcn'ectg''dghqtg'kv'chtgewu'y g's wcnkv{ ''qh'hktg0'Vj ku'xkukqp''ku'kp''uwr r qtv'qh'y g'' O krkct { 'J gcnj ectg''U{urgo '*OJ U+'Uvtcvgi ke''Hqewu''cpf ''S wcf twr rg'Cko ''qp''j gcnj ''cpf ''y gmpguu'' cpf ''eqo r rgo gpwu'y g'Cto { ''Rgthqto cpeg''Vtkcf 0'KEJ Røu'tgugctej ''ko r cevgf ''y g'4235'Co gtkecp'' J gctv'Cuuqekcvkqp'*CJ C+tCo gtkecp''Eqmgi g''qh'Ectf kqnqi { '*CEE+'Rtgxgpvkqp''I wkf grkpgu^{6''}cpf '' qpg''qh'KEJ Røu'r tgxgpvkqp'r krqv'o qf gnu'j cu''dggp''tcpurcvgf 'kpvq''r tcevkeg''eqo r rgo gpvkpi ''y g''WU'' Cto { ''Uvti gqp'I gpgtcnøu'Gzgewkkg'J gcnj ''cpf ''Y gmpguu''Rtqi tco 0

KEJ Røu'wnko cvg''i qcn'ku'vq'vtcpurcvg''qwt ''gxkf gpegf/dcugf 'tgugctej 'hkpf kpi u'hqt''cr r necvkqp''kpvq'' enkplecn'r tcevkeg''kp''cp''ghqtv'vq''cej kgxg''yj g'hqmqy kpi 'tgugctej ''cko u<''

- AKo r tqxg"Hqteg"J gcnj "d{"dgwgt"wpf gtuvcpf kpi "vj g"EXF "tkuniuwuegr vkdktw{ "qh'o ktkct {" ur gektke"r qr wncvkqpu"cu"y gm"cu"vq"wpf gtuvcpf "vj g"kpf kxkf wcn'ugtxkeg"o go dgt"vj tqwi j " ngcf kpi /gf i g"tgugctej "wukpi "pqxgn'vqqnu"cpf "vgej pqnqi kgu0"
- Akpxguvki cvg"cpf "etgcvg"vtcpuhqto cvkqpcn'o qf gnu"qh'j gcnyj ectg"f gnkxgt { 'vj tqwi j 'r gtuqpcnkj gf " EXF 'r tgxgpvkqp"vtcenu"cu"cp"cf lwpev'vq"vtcf kkqpcnlectg0"
- ÁTghkpg'kpf kxkf wcnk gf ''r tgxgp kqp''utcvgi kgu''y tqwi j ''uvcvkuvkecn'f cvc''o qf gnkpi ''vq''f ghkpg''y g'' o quv'equv/ghge kxg''cpf ''uwuvckpcdng''cr r tqcej gu'kp''r tqo qvkpi ''ectf kqxcuewrct''j gcnj '' y tqwi j qw''y g''o krksct { ''hkge {eng0'''
- AUko wncpgqwun{.'ko r tqxg'wpf gtuvcpf kpi "qh'yj g'o qrgewrct.'r j {ukqrqi kecn'dkqej go kecn'' ko o wpqrqi kecn'cpf "gpxktqpo gpvcn'dcuku"qh'ectf kqxcuewrct "*EX+'j gcnj "cpf "f kugcug''cpf ''q''

wug''y cv'wpf gtuvcpf kpi ''vq''f gxgrqr 'ko r tqxgf ''cr r tqcej gu''vq''f kugcug''f kci pquku.''vtgcvo gpv'' cpf ''r tgxgpvkqp.''kp''hpg''y kj ''P J NDKUtcvgi ke''Rrcp''422: 0''''

Body

Overall Program Initiatives

"

"

Qp'8'F ge''4235.''KEJ R'j grf ''ku''ugeqpf ''o ggvkpi ''qh''y gkt''Uekgpvkhe''Cf xkuqt { ''Dqctf ''*UCD+''kp'' y j kej ''ewttgpv'tgugctej ''kpkkcvkxgu''y gtg''tgxkgy gf ''cpf ''pgy ''f ktgevkqpu''qh'tgugctej ''cpf ''tcpurcvkqpcn'' qr r qtwpkkgu''y gtg''gzco kpgf 0'Vj ku''uweeguuhwn'o ggvkpi ''xcrkf cvgf ''KEJ Røu''hwwtg''uekgpvkhe'' tqcf o cr ''qp''dqyj ''y g''enkplecn'cpf ''o qrgewrct''rgxgr0''''

Vj g'hqmq kpi 'uki pkhecpv'ÆJ R'cej lgxgo gpu'uj qwf 'dg'' ki j rki j vgf 'kp'vj ku'tgr qtv0Cp'ÆJ R" o cpwætkr √''y cu'kpenvf gf 'cu'gxkf gpeg'\q'uwr rqtv'vj g"pgy 'Enlpkecn'I wkf grkpg"ej cpi g'\q'kpenvf g" hco kn('j knqt {'cu'c'uki pkhecpv'EXF 'tkunihcevqt'd{ 'vj g'Co gtkecp'' gctv'Cuuqekcvkqp"cpf 'Co gtkecp" Eqngi g'qh'Ectf kqnqi {'Gzr gtv'Rcpgrl4235'hqt''P gy 'I wkf grkpgu'kp'EXF 'Tkunicuuguto gpv0' Cff kkqpcm{.'wr qp'tgs wguv'qh'yj g'QVUI 'qh'yj g'Cto {.'KEJ R'j cu'f gxgnqr gf 'c'ewuxqo k gf 'o qf grl hqt'Gz gewkxg''J gcnj 'vq''cf f tguu'kurwgu'tgrgxcpv'vq''qwt'pcvkqpøu'hg'ExF ''Tkunicuuguto gpv0' Vy q'kpygtcevkxg''cpf 'gf wecvkqpcrl'y qtmij qr u'cmpi 'y kj 'r gtuqpcrk gf 'hkguv{ rg''r tguetkr vkqpu'hqt'' gcej 'ngcf gt''cpf lqt'ur qwug'y gtg''r tqxkf gf 'y kj 'c'j ki j 'ngxgrl'qh'ucvkuhcevkqp'htqo 'vj g''Uwti gqp'' I gpgtcr0Nkgwgpcpv'I gpgtcrlRcvtkekc''J qtqj q'tgeqi pk gf ''KEJ Rø'nhwn'uwr rqtv'qh'y g'O J U'' uvtcygi le'hqewu'qp''J gcnj ''cpf 'Y gmpguu.''y j gp'uj g''uvcyf 'y cv'öKEJ R''r tqxkf gu'c''r j gpqo gpcrl' o qf grlht' l'pkkkcvkpi 'kpvgi tcvkxg'y gmpguu''r tqi tco u''yi tqwi j qw'yi g''o krkct {0'Vj g''gxkf gpeg/dcugf '' crr tqcej ''qh'y g''EJ R''gco ''eqo r nko gpwl'o krkct{ 'o gf lekpg06''Kp''j gt''yguvko qp{''q''Eqpi tguuø'' J qwug'Crr tqr tkcvkqpu'Eqo o kwgg''qp''Cr tkrl4.''4236.''NVI ''J qtqj q'ucvgf 'öKEJ R'ku''y g''qpn{''EQG'' y cv'ur gekhecm{''cff tguugu''qduvcergu'tgrcyf''q'' gcnj {''nkkpi 'kp'y g''o krkct{0'KEJ R'ku'' u{pej tqpk gf ''y kj ''Cto {''O gf kekpgøu''o qxgo gpv'vq'ko r tqxg'' gcnj (0⁸''</sup>

Vq'dgwgt'tghgev'KEJ Røu'tqng'kp''qxgtcm'y cttkqt'j gcnj."õEctfkqxcuewnct'Rtgxgpvkqp'Rtqi tco " *ERR+ö'j cu'dggp''ej cpi gf '\q'õEctfkqxcuewnct'J gcnj 'Rtqi tco "*EJ R+ö0O ctngvkpi 'o cvgtkcnı." r tqi tco 'hqto u''cpf ''r tqvqeqnı'tgxkukqpu'\q'tghgev''y g''pgy ''pco g''ctg'kp''r tqi tguu0''

Vj g'hqmqy kpi 'uxchh'cf f kkqpu'kp''y g'r cuv'{gct''y kn'dg'kput wo gpvcn'kp''qwt 'cdktkv{ ''q''o qxg'hqty ctf '' y kj ''qwt ''ewttgpv'tgugctej 'r qt vhqhq''cu''y gn'cu'kp''y g'f guki p''qh''pgy ''cpf ''pqxgn'uelgpeg<"'' □Æctf kq/Ko o wpqmi { ''Rj {ukekcp'Eqpuwncpv'y kj ''cp''gzr gt vkug'kp'kphrco o cvqt { ''o ctngtu''cu'' r tgf kevqtu''qh''cy gtquengtqvke''f kugcug''y kn'dg''kput wo gpvcn'kp'f guki pkpi 'hwwtg''KEJ R'r tqvqeqn0'

I tgi kevitu qire y giqueigiq ve i kigetig y kilog you wo governo i gux pipi i iwwig kesi ki i quequo Avweqo gu'F cvc'Ur gekenkuv'y kni'r wtuwg'y g'KEJ R'F cvc'O cpci go gpv'Rrcp''q'o gti g'f cvc'htqo " wy q'r tgxkqwu'f cvcdcugu'kp''qtf gt''q''o qxg''hqty ctf 'y kj "qpg'f cvcugv'hqt''hwty gt''cpcn{uku." kpenwf kpi ''322' ''s werkv{ "cuuwtepg''qh'f eve0'

 $\Box \hat{A}_{q}$ Appqi tcr j gt 'y km'eqpf wev'dq y "ectq kf 'wn tcuq wpf "cpf "gej qectf kqi tco u'hqt 'r tq vqeq n0" "

Kp'ý g'r cuv's wetvet. 'ý g'KEJ R'Gz gewkk g'Vgco 'y cu'cevk gn{ "gpi ci gf "kp'ý g'uwdo kuukqp'qh'qwt''H[" 4237/423; 'tgugetej 'r tqr quen0'Vj ku'uwdo kuukqp'kpenwf gu'qpi qkpi 'KEJ R'tgugetej 'dw'enq'ý g'' f guki p'qh'e'pgy 'KEJ R'tepf qo k gf. 'eqpvtqmgf 'repf o etm'r tqvqeqn'd{ 'vj g''eetf kq/ko o wpqmi kuv' r j {ukekep''eqpuwnepv'y kj 'e'hqewu''qp''i gpf gt''epf ''dkqo etmgtu''eu''r tgf kevqtu''qh''evj gtquergtqvke'' f kugeug0'''

Task #1: Complete the "Better Adherence to Therapeutic Lifestyle Change Efforts (BATTLE) Trial".

<u>O gyi qf qrqi {</u>"

Vj g''r wtr qug''qh'y ku'uwf { 'ku''q'f gygto kpg'y j gyj gt''npqy ngf i g''qh''cdpqto cn'tguwnu'htqo 'c'' pqpkpxcukxg''yguv'hqt'f gygevkqp''qh'uwdenkpkecn'cyj gtquengtquku'*EKOV+.'kp''cf f kklqp''q''npqy ngf i g''qh'' EXF 'tkumhcevqtu.''gpj cpegu''cf j gtgpeg''yq''j gcnyj { 'hthguv{ ng''dgj cxkqtu'kp''eqo r ctkuqp''yq''qpn{ 'EXF '' tkumhcevqt''npqy ngf i g0'Vj g''uwf { ''y km'dg''eqpf wevgf ''y kyj 'kpf kxkf wcm''cv'o qf gtcvg''yq''j ki j ''tkumhqt'' ectf kqxcuewrct ''gxgpvu''dcugf ''qp''EXF ''tkumhcevqt''r tqhkng''cpf ''gxkf gpeg''qh''uki pkhecpv''uwdenkpkecn'' cyj gtquengtquku0'''

Vj ku'vy q/cto .'f qwdrg/drkpf gf 'uwf { 'y kn'tcpf qo k g'uwdlgevu'\q''gkj gt'tgegkxg'E KO V'tguwnu'*T/ EKO V'I tqwr +'qt'j cxg'E KO V'tguwnu'y kj j grf '*Y /EKO V'I tqwr +'kp''y g'ugwkpi ''qh'c'5/o qpyj ''VNE '' kpvgtxgpvkqp0Chgt''y g''5/o qpyj ''VNE ''kpvgtxgpvkqp'r gtkqf 'ku'eqo r ngvgf .''uwdlgevu'y j q'j cf ''E KO V'' tguwnu'y kj j grf 'y kn'tgegkxg''y ku'kphqto cvkqp0Dgecwug''npqy ngf i g''qh'y g''uwf { ''j { r qvj guku''eqwrf '' ko r cev'y gkt''dgj cxkqt'f wtkpi ''y g''khguv{ ng'kpvgtxgpvkqp.''uwdlgevu'y kn'dg''drkpf gf ''\q'' y g''uwf { '' j { r qvj guku0'Uko krctn{ .'tgugctej ''uvchh'ko r ngo gpvkpi ''y g''VNE ''kpvgtxgpvkqp'y kn'dg''drkpf gf ''\q'' uwdlgevu@tcpf qo k cvkqp''cuuki po gpv0'''

KVku'j {r qvj guk gf 'vj cv'r ctvkekr cpvu'y ky 'EXF 'tkunihcevqtu'y j q'j cxg'mpqy ngf i g'qh'vj gkt 'qy p'' EKO V'vguv'tguvnu'uj qy kpi 'uki pkhecpv'uvdenkplecn'cvj gtquengtquku'y knih go qpuvt cvg'dgvgt'' cf j gtgpeg'vq''VNE 'vj cp''yj qug'uvdlgevu'htqo 'y j qo 'vj g'EKO V'vguv'kphqto cvkqp'ku'y ky j gnf 0'C'' eqo r qukkg'kpf gz ''qh'cf j gtgpeg'vq''y g''VNE 'kpvgt xgpvkqp''y cu'ugrgevgf ''cu''y g''r tko ct { ''qweqo g'' o gcuvtg''ukpeg''yj g''o ckp''i qcn'qh'yj ku'uvwf { ''ku''vq''cuuguu''yj g''ko r cev'qh''EKO V''ko ci kpi ''npqy ngf i g''qp'' ej cpi g'kp'hkguv{ng'dgj cxkqtu0''

C "eqo dkpgf "o gcuwtg"qh"cf j gtgpeg. 'tghrgevkpi "dqyj "cur gewl"qh'vj g"htguv{ ng"kpvgtxgpvkqp" *O gf kgttcpgcp/v{r g"f kgv."o qf gtcvg"cgtqdke"gzgtekug+.'y cu"ej qugp"vj cv'wugu"ceegr vgf "o gcuwtgu"qh" f kgv"cpf "gzgtekug"cf j gtgpeg"tgr qtvgf "kp"vj g"htgtcwtg0"Ugeqpf ct { "qweqo gu"kpenwf g<3+" Cf j gtgpeg"vq"gcej "r tqi tco "eqo r qpgpvu=4+"Ej cpi gu"kp"o qf khcdng"EXF "tkumhcevqtu"cpf "qyj gt" dkqej go kecn'o ctngtu=5+"Go qvkqpcnhcevqtu"uwej "cu"cpzkgv{."ugh/ghhkece{."o qvkxcvkqp."cpf "6+" Cy gtquengtquku"cpf "EKO V"Mpqy ngf i g"Cuuguuo gpv"Ueqtg"*qpn{"kp"EKO V/T "uvdlgevu+0

TguwnulEqpenwukqpu-

"

 $\frac{1}{Mg} = \frac{1}{1000} \frac{1}{1000$

<u>Status:</u> O cpwuetkr w''ctg''dgkpi 'hkpcnk gf 'hqt''uwdo kuukqp0'Uwf { "enquwtg''f qewo gpwi'y gtg''cr r tqxgf " d{ "Y TPOOE''KTD''qp''47''Qevqdgt''4234''cpf 'hqty ctf gf ''vq''WUCOTOE''J TRQ0'''

Manuscripts in preparation:

□Álcwo 'P U.'J cnug{"IH''Y cnų gt'GO.'Xgtpcnu'O P 0Gzr nqtkpi 'vj g'tqng'cpf 'ko r cev'qh'nko kgf " o kpf hwnpguu'vtckpkpi 'kp''ej cpi kpi 'f kgv'cpf ''gzgtekug'dgj cxkqtu0*Kp'r tgr ctcvkqp+"

□ Á cn¼ gt 'GO. "Xgtpcnku'O P 0'F qgu'xkuwcn'mpqy ngf i g''qh'kpetgcugf 'tkumihqt''ectf kqxcuewrct'' f kugcug''chhgev'hkguv{ ng''ej cpi g''r tqi tco ''cf j gtgpegA'*Kp''r tgr ctcvkqp+''

Abstract Published/Presented as Poster<"

Y crl{ gt'GO .'Xgtpcrlu'O P .'O qf rlp'TGOllphwgpeg'qh'E IO V''cu''c''o qvkxcvqt'hqt'j gcnj 'dgj cxlqt'' ej cpi g'lp''c'j gctv'j gcnj ''r tqi tco 0'*Circ*. 4236=34; <CR3480*AHA EPI/NPAM 2014 Scientific Session.''Ucp''Htcpekueq.''EC.''O ctej ''3; .''4236+''

Cduxtcev"

Introduction: 'Ectqvkf 'kpvko c'o gf kc''y kenpguu'*EKO V+'wntcuqwpf 'ku'c'mpqy p'uwttqi cvg'o ctngt" qh'cy gtquergtquku'dw'hgy 'uwwf kgu''gzco kpg''ku'kphwgpeg''qp''r cvkgpv'dgj cxkqt0O qvkxcvkqp''cpf 'ugn/ ghkece{ '*UG+'ctg''mpqy p''r tgf kevqtu''qh'j gcnj ''dgj cxkqt ''ej cpi g0'Vj ku'tcpf qo k gf .'f qwdrg/drkpf '' vtkcn'gzco kpgf ''3+'wug''qh'EKO V'ko ci gu''r nwu''cuuqekcvgf ''EXF ''tkuni'vq''o qvkxcvg''cf j gtgpeg.''cpf ''4+'' y g''r tgf kevkxg''cdkrkv{ ''qh'o qvkxcvkqp''cpf ''UG''qp''cf j gtgpeg''ej cpi g0'

Methods: Rcvkgpvu'y kj '×'4'ectf kqxcuewrct'f kugcug'*EXF +'tkumlkcevqtu'cpf 'uwdenkplecn' cy gtquengtquku'y gtg''cuuki pgf 'vq''gkj gt'y g'kpvgtxgpvkqp'i tqwr '']tgegkxg'tguwnu'y ggm{ '*T/EKOV+_" qt''eqpvtqn'i tqwr '']y kj j qnf 'tguwnu'*Y /EKOV+_0Cm'r cvkgpvu'tgegkxgf ''c''34/y ggmlrkhguv{ng'' tqi tco '' *O gf kgttcpgcp''f kgv.''cgtqdke''gzgtekug.''i tqwr 'uwr r qtv40Qxgtcm'ej cpi g'kp''cf j gtgpeg'htqo ''dcugnkpg'' vq'y ggml34''y cu'f gvgto kpgf ''wukpi ''cp'CPEQXC''o qf gn'y j gtg'' ''cf j gtgpeg'y cu'c''eqo r qukg'' o gcuwtg''qh'f kgv'cpf ''gzgtekug''cf j gtgpeg0'Kpkkcn'o qvkxcvkqp''r nwu''gzgtekug''cpf ''pwtkkqp''UG''y gtg'' cuuguugf ''q'f gvgto kpg''y gkt''r tgf kevkxg''cdktk{ ''qh'cf j gtgpeg'kp''c''uvcpf ctf 'tgi tguukqp''o qf gn0''

Results: 388'r cvkgpwi'tcpf qo k gf = 383'*T/EKO V'p?: 3='Y /EKO V'p?: 2+'grki kdrg'hqt'kpvgpvkqp/vq/ vtgcv'cpcn{uku0Rcvkgpui'y gtg'o kf frg'ci g'*o gcp''ci g''? '76'Õ'33''{tu+:'84' '*322''qt''383+'y qo gp." 6: '*99''qh'383+''drcen0'Dcugrkpg''i tqwr 'f khbgtgpegu<'Y /EKO V'i tqwr 'y cu''{qwpi gt '*74'xu''77''{tu='' r?2027+:'j cf 'c''nqy gt'u{uvqrke''dmqf ''r tguuwtg'*342''xu''347='r?2023+:''nqy gt'' ''hco kn{''j knvqt {''qh'' EXF '*6; ''xu''87='r?2025+0'Kp''eqo r ctkpi ''T/EKO V''xu''Y /EKO V'i tqwr u.''pq''f khbgtgpeg'y cu''f gygevgf '' kp''qxgtcm'' ''cf j gtgpeg''ej cpi g'*3806''Õ'4708''xu''3; 0 'Õ'4706='r?205; +0'Kpkxcn'o qvxcvkqp''cpf ''UG'' o gcuwtgu'y gtg''pqv''r tgf kevkxg''qh''ej cpi g''kp''cf j gtgpeg''y j gp''cf f gf ''q''i tqwr ''cuuki po gpv'*ugg'' Vcdrg+0''

"	R/Xcnwg"*Tgitguukqp"Eqghhkekgpv+"					
O qf gn'	ЕЮV'I tqwr"	Gzgtekug"	P wtkkpp"	Kokvken'		
		UG''	UG''	Oqvkxcvkqp"		
Cf j gtgpeg'Ej cpi g, "? 'EKO V'i tqwr ''- ''	20665"	"	"	20899"		
Kokkcn'Oqvkxcvkqp"						
Cf j gtgpeg'Ej cpi g, "? 'EKO V'i tqwr "'- "	20636"	20,49"	209:6"	"		
Gzgtekug"UG ³ "- "P wtkkqp"UG ³ ""						
Cf j gtgpeg'Ej cpi g, "? 'EKO V'i tqwr ''- "	2068; "	209;:"	20797"	20774"		
Kokkcn'Oqvkxcvkqp"- "Gzgtekug"UG ³ "-"						
P wtkkqp"UG ³ "						
, Cfj gtgpeg"ej cpi g'y cu'eqo r wgf "d{"cfj gtgpeg"*ecr r gf "cv'322' +"cv'y ggn'340						
³ Dcugrkpg"gzgtekug"cpf "pwtkkkqp"UG"ctg"ed	qpulf gtgf "eqxctk	cvgu()'				

Conclusions: 'EKO V'gxkf gpeg''qh'uwdenkpkecn'cyj gtquengtquku'kpetgcugf 'r ctvkekr cpv'EXF 'tkum' cy ctgpguu'dw'f kf "pqv'vtcpurcy"kpvq''cevkqpcdng'j gcny { "dgj cxkqt''ej cpi gu'dg{qpf 'vj qug'kp''yj g'' eqpvtqn'i tqwr 0P gkyj gt "gz gtekug"pqt''f kgvct { "cf j gtgpeg'y cu''chbgevgf ''d { 'kpkkcn'o qvkxcvkqp''qt''ugnh' ghtkece { ''y j gp''cf f gf ''vq''EKO V''tkum'cy ctgpguu0'''

Task #2: Complete the CADRe Five-Year Follow-up Protocol.

<u>Ogyiqfqmqi {</u>"

Vj ku'hqmqy /wr 'uwwf { 'y km'f gvgto kpg''y g'r gtukuvgpeg''qh'j gcnj { 'hklguv{ ng'dgj cxkqtcn'ej cpi gu'cpf " EXF 'tkumhcevqt''eqpvtqn'tguwnu'chvgt''y gkt''qtki kpcn'ECFTg''uwwf { 'r ctvkekr cvkqp0'Vj ku''uwwf { 'y km' eqpvkpwg''cu''c''nqpi kwwf kpcn'qdugtxcvkqpcn'uwwf { 'y j gtg'r cvkgpwi'y km'j cxg''{gctn{ 'hqmqy /wr 'xkuku''cv' 3.''4.''5.''6.''cpf ''7''{gctu''chvgt''eqo r ngvkqp''qt''gzr gevgf ''eqo r ngvkqp''qh'y g'ECFTg''Uwwf { 0'Vj ku''uwwf { '' y km'kpxqnxg'r tqur gevkxg''eqngevkqp''qh'f cvc0'Cm''eqngevgf ''f cvc'ku''eqpukf gtgf ''Y TPOOE'' Ectf kqmi { ''uvcpf ctf ''qh''ectg''hqt''y g''uwwf { ''r qr wncvkqp''kf gpvkhkgf 0''

K'ku'j {r qvj guk gf ''y cv'r ctvkekr cpvu'y j q'j cxg''dggp"gzr qugf ''q''cp''kpvgpukxg''htguv{ng''ej cpi g'' r tqi tco ''y kn'f go qpuvtcvg''nqpi /vgto ''ectt {qxgt"qh'j gctv'j gcnj { ''ej ctcevgtkuvkeu''kpenvf kpi '' r gtukuvgpeg''qh'hcxqtcdng''htguv{ng''ej cpi g''dgj cxkqtu''cpf ''tkunihcevqt''eqpvtqn0Wr ''q''385''o cng''cpf '' hgo cng''ECF Tg''uwwf { ''r ctvkekr cpvu.''ci g''3: ''{gctu''qt ''qnf gt.''y kj ''uwdugs wgpv''eqo r ngvkqp''qh'''Rj cug''3'' qh''y g''ECF Tg''Uwwf { ''s5/o qpy ''f cvc''eqngevkqp+'y gtg'tg/eqpvcevgf ''cpf ''kpxkgf ''q''r ctvkekr cvg''kp'' y ku''7/{gct''hqmy /wr ''uwwf { ''s'r quv/uwwf { ''eqo r ngvkqp''qt''gzr gevgf ''eqo r ngvkqp+0''''

C''eqo r qukg'kpf gz''qh'9''j gcty'j gcnj {''ej ctcevgtkukeu'*DO K3: (7''6''47="NF N/ej qnguvgtqn'>'322'' o i lf N='f kgvct { 'hkdgt'kpvcng'×''47'i o ulf c {='eqpuwo r vkqp''qh'7''qt''o qtg'htvku''cpf ''xgi gvcdngu''r gt'' f c {='DR'>''3621; 2''o o J i ='tgi wrct''gzgtekug'×''372''o kp ly ggm''cpf 'f ckn{ ''r tcevkeg''qh'ECF Tg'' r tqi tco ''uvtguu''o cpci go gpv'vgej pls wgu+''y cu''ugngevgf ''cu''y g''r tko ct { ''qweqo g''o gcuwtg''ukpeg''y g'' o ckp''i qcn'qh'y ku''uwf { 'ku''q''cuuguu'y g''r gtukuvgpeg''qh'hkbguv{ ng''ej cpi g''dgj cxkqtu''cpf 'tkunhcevqt'' eqpvtqn0'Vj g''J gctv'J gcnj ''Kpf gz ''*J J Kt.''r tgugpvgf ''cu''c''ukpi ng''ueqtg'*tcpi g''2/9+.''y kn'dg''cuuguugf '' q''gcej ''uwdlgev'{ gctn{ 0'Cf f kkqpcm{.''gcej ''qh''y g'9''j gctv'j gcnj { ''ej ctcevgtkukeu'y kn'dg''cuuguugf '' kpf gr gpf gpvn{ ''cu''c''eqpvkpvqwu''xctkcdng0'Ugeqpf ct { ''qweqo g''o gcuwtgu'kpenvf g<''Ej cpi gu'kp'' o qf khcdng''EXF ''tkunhcevqtu''*dnqf ''r tguuwtg.''dqf { ''eqo r qukskqp''cpf ''hkpguu.''hr kf ''ngxgnu''cpf '' i nwequg+=''E/tgcevkxg''r tqvgkp''cpf .''S wcfk{ ''qh'Nkhg0'

<u>TguwnulEqpenwukqpu</u>

<u>Status</u>: Uwf { "enquwtg"f qewo gpwl"cr r tqxgf "d { "Y TPOOE 'F TR"qp"34 'O ctej "4235"cpf " cr r tqxgf "d { "WUCOTOE 'QTR"J TRQ"qp"39 'O c { "42350'O cpwuetkr v'r tgr ctcvkqp"ku'kp"r tqi tguu0'

Task #3: Continuation of the "Comprehensive Cardiovascular Risk Assessment and Prevention Program (CHP)" at WRNMMC.

<u>Methodology</u>

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Vj ku'r tqi tco "ugtxgu'cu'c'r ncvhqto "hqt "qpi qkpi "vtcpuncvkqpcn'tgugctej "cevkxkkkgu."c'öxktwcn" ncdqtcvqt {ö'dcugf "qp'uekgpvkhke"hkpf kpi u'hqt "yj g'f gxgnqr o gpv'qh'dguv'r gtuqpcnk gf 'r tgxgpvkxg" r tcevkegu0'Kp"qvj gt 'y qtf u."vj g'r ncvhqto "cmqy u'KEJ R'vq'i cvj gt "cp"gzr cpukxg"pwo dgt "qh'f cvc"r qkpvu" hqt"gcej 'r cvkgpv'qt 'uwdi tqwr "qh'r cvkgpvu'*gxgpwcm("eqo dkpgf 'y kj "'f cvc"cv'c"o qngewrct"ngxgn+" yj cv'y j gp"ngxgtci gf 'y knitguwn/kp"yj g"etgcvkqp"qh'pgy "vqqnu"kp"vgej pqmqi { 'vq"f ghkpg"y gmpguu." r tgf kev'cpf 'r tgxgpv'f kugcug. "cpf "go r qy gt 'r cvkgpvu'cpf 'r tqxkf gtu'vq"vtcpuhqto 'vj gkt 'j gcnj ectg0""

Vj g'EJ R'r nevhqto 'j cu'c'f wen'r wtr qug'epf 'ku'o wnkhwpevkqpen0'Vj ku'r nevhqto '3+'enqy u'hqt'' o wnkr ng'tgugetej 'r tqvqeqni'vq'dg'eqpf wevgf 'cu'kv'ugvu'yj g'uvei g'hqt'tgetwkso gpv.'gptqmo gpv'epf "

j {rqvjguku'i gpgtcvkqp."cfxcpegf"fcvc"oqfgnkpi"cpf"ukownxcpgqwun{"4+"rtqxkfgu"c"xgpwg"yjgtg" tgugctej 'hkpf kpi u'htqo ''y gug''r tqvqeqnu'ecp''y gp''dg''yguygf. ''xcnkf cygf ''cpf ''tcpurcygf ''kpvq'' crrnkecvkqp'hqt"enkplecn'r tcevkeg0Qwt"r tqvqeqnu'y kj kp''y g'EJR''ctg''ur gekhlecm{ "f guki pgf ''vq" gz co kpg''y g'ghhgevu'qh'qwt''o krksct {øu'j ki j ''qr ''vgo r q''y j kej ''r tgf kur qugu''qwt ''ugt xkeg''o go dgtu''vq'' ceegrgtcvgf "cyj gtquengtqvke"tkumitguwnkpi "htqo "j ki j "uvtguu. "RVUF. "f gr tguukqp. "urggr "kpuwhikekgpe{." qxgty gki j v."rtgf kcdgvgu"cpf "rtgj {rgtvgpukqp"co qpi "qvj gt"vtcf kkqpcn"f kugcug"tkum"hcevqtu0"""

Vj ku'r tqi tco 'y cu'guvcdrkuj gf 'vq'cfftguu'y g'vpks wg'pggfu'qh'o krkwct { 'dgpghkekctkgu'cv'tkurthqt'EX'' f kugcug0K/k/penwf gu'eqpxgpvkqpcn'cpf 'pqxgn'EX'tkum'r tqhkrkpi "*j gcnj "cuuguuo gpvu. "rcdu. "o ctngtu." y getedng'o qpkqtu+'empi 'y kj 'vekqtgf 'epf 'r gtuqperk gf 'dgj exkqteritgeqo o gpf evkqpu'hqt'' r tko ct { "qt "ugeqpf ct { "r tgxgpvkqp"d { "cp"kpvgi tcvkxg"vgco "qh'r tqxkf gtu"eqo r tkugf "qh'c"ectf kqrqi kuv." urggr "ur gekenkuv."pwtug"r teevkkapgtu. "pwtkkapkuvu. "uvtguu"o epci go gpv"kpuvtvevatu"epf "gzgtekug" rj {ukqnqi kuvu0Xcnkf cvgf "vqqnu'vq"uetggp"hqt"cpf "o gcuwtg"EX"tkum'ctg"r ctv'qh'vj ku'kpenwukxg" r cemci g0T gr qtv'ectf u'hqt''y g'r cvkgpv'cpf 'r tqxkf gt 'cu'y gm'cu'go ckripqvkhecvkqpu'ctg'wkrkt gf 0Vj g" r tqi tco "ku"cp"cf lwpev'\q"y g"dguv'o gf kecn'r tcevkegu"r tqxkf gf "d{ "y gkt"r tko ct { "ectg"r tqxkf gt0Wr vq'3222'r cvkgpvu'o c{''dg"gptqmgf "gcej "{gct0'Uqo g"qh'yj g'r cvkgpvu'*uvej "cu"pwtugu"qt 'vtcwo cvke" kplwt {"r cvkgpvu."gve0#"o c {"dg"kp"uwdi tqwr "r tqi tco u"dgecwug"qh"wpks wg"pggf u0'Vj g"EJ R"ugtxgu"cu"c" r revhato "hat"qpi qkpi "vtcpurcvkqpcn"tgugctej "cevkxkkgu."c"õxktwcn"redatcvqt {ö"hat"vj g"f gxgrqr o gpv" qh'dguv'r tgxgpvkxg'r tcevkegu''cpf "hqt 'EX"gf wecvkqpcn'cpf "o ctngvkpi "o cvgtkcnu0

Vj g'õQweqo gu'qh'yj g'ERR'Rtqi tco ö'r tqvqeqn'r tqxkf gu'hqt'tgvtqur gevkxg'gzco kpcvkqp''qh'gzkuvkpi " f cvc'hqt''y g'r wtr qug''qh'gzco kpcvkqp''cpf 'tgr qtvkpi ''qh''y g'tguwnu''qh''y g'gxcnvcvkqpu''cpf 'kpvgtxgpvkqpu'' qh'y g'EJ R0Vj g'cppwcn'eqpvkpwkpi 'tgxkgy '*ET+'y cu'crrtqxgf ''d{ 'Y TPOOE'KTD''qp''44'Crt''360C'' Ej cpi g"qh'RKco gpf o gpv'htqo "EQN'Tcpf qrr j 'O qf nkp. 'O E. "WUC "vq 'NVE "Vqf f "Xkmkpgu.'O E. "WUC" y cu'uwdo kwgf "vq"Y TPOOE "KTD"cpf "crrtqxgf "cu"qh'8"Cwi "42360"Vj gug"crrtqxcnu'y gtg"hqty ctfgf " vq'J TRQ'xkc'J IH0"

Status:"""

"

Vqvcn'r cvkgpv'xkuku'f wtkpi 'r cuv' {gct <3; 98 * kpenwf gu'vgrgr j qpke 'eqcej kpi 'ecm+''

Manuscripts-Published (See Appendix A): A Golcuuqp'C. "Mcuj cpk'O."O qf olp'T."J qy ctf 'T. "Xgtpcolu'O 0'Hcvki wgf "qp"Xgpwu."Unggr { "qp" O ctuô I gpf gt "cpf "tcekcnif khgtgpegu"kp"u{o r vqo u"qh'urggr "cr pgc0'Sleep Breath. 4236"O ct" 370']Gr wd"cj gcf "qh'r tkpv_"

Manuscript-In-preparation:

EA Mcuj cpk'O. 'Grkcuuqp'C. 'O qf rkp'T. 'Xgtpcrku'O 0'Ectf kqxcuewrct 'J gcnyj 'Rtqi tco 'Kpetgcugu'' Ugth/Ghhlece $\{0'\}$

Mg{"U{orvqo"kp"Gxcnxcvkqp"qh"Urggr"Crpgc0'CHEST."Qev'4236="Cwrkp."VZ0"

Cduxtcev"

Purpose: Tgegpvn{ "r wdnkuj gf "i wkf gnkpgu"hqt "o cpci go gpv"qh"qduvt wevkxg"urggr "cr pgc"*QUC+" gpf qtug "gx cnxc vkqp" qh'urggr kpguu'y ky "y g'Gr y qt y "Uecng" dw'f q "pqv'uwi i guv'y g''cuuguuo gpv'qh" hcvki wg0Rtkqt'tgugctej "qp'i gpf gt'f khgtgpegu'kp'QUC'u{orvqou'j cu'uj qy p'eqphrkevkpi 'tguwnu'kp'' r ctv'dgecwug'u { o r vqo 's wguvkqppcktgu'j cxg'pqv'kpenwf gf 'hcvki wg'cpf 'kp'r ctv'dgecwug'QUC 'y cu'

f gygto kpgf "d{"uetggpkpi "s wguvkqppcktg"pqv'd{"i qrf "uxcpf ctf "qxgtpki j v'r qn{uqo pqi tcr j {0"Y g" uqwi j v'vq"enctkh{"kh'u{o r vqo u'f khhgtgf "d{"i gpf gt "kp"uwdlgewu'y kj "QUC"eqphkto gf "d{"qxgtpki j v" r qn{uqo pqi tcr j {"wkrk kpi "u{o r vqo /ur gekhke"s wguvkqppcktgu0"

Methods: Qh'uwdlgeut'gpythpi "c'ectf kqxcuewrt'f kugcug''r tgxgpykqp'tgi knt {.'y g'i cyj gtgf 'f cxc"qp" f go qi tcr j ku'cpf 'urggr/tgrcygf 'u{o r vqo u'hqt'eqpugewkxg''r cxkgput'y j q'wpf gty gpv'f kci pquke" r qn{uqo pqi tcr j {0QUC ''y cu'f ghpgf ''y kj ''c'tgur ktcvqt { 'f kuwtdcpeg'kpf gz '*TF K#qh'×'7"gxgput'' r gt ''j qwt0'Urggr kpgut'y cu'tgeqtf gf ''wukpi ''y g'Gr y qtyj ''Uecrg'*GU.'tcpi g''2''q''46+0'Hcvki wg'y cu'' o gcuwtgf ''y kj ''y g''Ucphqtf 'Hcvki wg''Uecrg'*HU.'tcpi g''2''q''32+0'Uwdlgeut'y kj ''cpf ''y kj qw'QUC'' y gtg''eqo r ctgf ''d{ ''i gpf gt 'hqt''u{o r vqo u'qh'hcvki wg''cpf ''f c{ vko g'urggr kpgut''d{ ''v vguv0 **Results:** Qh'84''eqpugewkxg''uwdlgeut'*62''y qo gp.''o gcp''ci g'790603408''{gctu+'GU'y cu'32020609." HU'y cu'60, 030, 0Y kj ''pq''QUC.''GU'kp''y qo gp'*: 04060 +'y cu''pqv'f khgtgpv'htqo ''o gp'*; 070602." r ?2085+'cpf ''HU'kp'y qo gp'*32060706+'y cu''pqv'f khgtgpv'htqo ''o gp'*7020504.''r ?209; +0J qy gxgt." y kj ''QUC.''GU'kp'y qo gp'*32060706+'y cu''uko krct''q''o gp'*32070702.''r ?20,5+0'Vj ku'i tgcvgt''f gi tgg''qh'hcvki wg'' kp'y qo gp''y kj ''QUC''y cu'hqwff 'f gur kg'c''rceni'qh'uxckukecni'f khgtgpeg'kp''r qn{uqo pqi tcr j kcni' xctkcdrgu''dgw ggp'y qo gp''cpf ''o gp''hqt'' C''pe4+.''ctqwucn'kpf gz'*'r ?2082+.''cpf''' vko g>; 2' '''u wwtcvgf '''r ?208: +0'

Conclusions: Kp''y ku'o qf gtcvg/uk gf ''eqj qtv'qh''uwdlgevu''y kj ''QUC''xgtkhgf ''d { ''r qn{uqo pqi tcr j {." y qo gp''gzr gtkgpegf 'hcvki wg''o qtg''eqo o qpn{ ''y cp''f kf ''o gp''gxgp''y j gp''qdlgevkxg''o gcuwtgu''qh'' QUC''ugxgtkx{ ''y gtg''uko krct0'Vj ku'hkpf kpi ''dtqcf gpu''qwt''wpf gtuvcpf kpi ''qt''j qy ''i gpf gtu''o cpkhguv'' u { o r vqo u''qh''QUC''f khhgtgpvn{0

Clinical implications: Rtqxkf gtu'ecp'dgwgt''ecr wtg'QUC 'kp'y qo gp'd { "wukpi 'y g'r tqr gt" s wguvkqppcktg''qqn'\q'uetggp'hqt'hcvki wg. "pqv'tgn{ kpi 'uqngn{ "qp''cuuguuo gpvu'qh'urggr kpguu0'Hwwtg" enkpkecn'i wkf gnkpgu'uj qwrf 'kpeqtr qtcvg''y ku'tgeqo o gpf cvkqp''q''cxqkf 'wpf gt/tgeqi pkkqp''qh'urggr " r cy qmqi { 'kp'y qo gp0'

Abstract Submitted for Poster Presentations:

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Harding C. 'Grkeuuqp'C. 'Gpi ngt 'T. 'Hwngt 'E. 'Xgtperku'O 0'Rtgj {r gtvgpukqp'eqgzkuvu'y kj 'EXF '' tkumhcevqtu0'AHA Scientific Session 20140'P qxgo dgt '42360'

Cduxtcev"

Introduction: "Vj g'o quv'tgegpv'i wkf grkpgu'hqt 'vj g'o cpci go gpv'qh'dmqf 'r tguuwtg'*DR+'uqrgn{" cfftguu'j {r gtvgpukqp. 'pq''mpi gt'eqpukfgtkpi 'vj g'encuukhecvkqp''qh'r tg/j {r gtvgpukqp0'Uwdlgevu'y j q" f q''pqv's wcrkh{ ''cu'j {r gtvgpukxg''dw'j cxg''c''o qf guv'kpetgcug'kp''DR''ctg''wptgeqi pk gf 'f gur kg''y gkt'' r qvgpvkcrihqt''ectfkqxcuewrct 'f kugcug'*EXF+'tkun0''

Objective: "Y g"gzco kpgf 'ý g"EXF ''tkmi'r tqhkg"qh'uwdlgewi'y ký ''o qf guv'DR"grgxcvkqp''q" f gygto kpg"ý g"r tgxcrgpeg"qh'tkmihcevqtu"cpf ''q'kf gpvkh{ ''cti gwi'hqt'kpvgtxgpvkqp0' **Methods:** Eqpugewikxg"uwdlgewi'gpvgtkpi ''y g"kpvgi tcvkxg"Ectf kce''J gcnj ''Rtqlgevøu''34/o qpvj ''EXF '' Tkmi'T gf wevkqp"T gi knt { ''y gtg"cuuguugf 'hqt"cpvj tqr qo gvtkeu''cpf ''c''EXF/tgrgxcpv'rcd''r cpgr0'' Uvdlgevu'y gtg"ecvgi qtk gf ''cu''pqto qvgpukxg'*DR≥3421: 2+:'r tg/j { r gtvgpukxg'*DR@421: 2''cpf '' >3621; 2+''cpf ''j { r gtvgpukxg''*DR@621; 2+0''Y g"eqo r ctgf ''pqto qvgpukxg''wdlgewi'y kj ''r tg/ j { r gtvgpukxg''cpf ''j { r gtvgpukxg''wdlgewi'hqt''f kthgtgpegu'kp''EXF ''tkmihcevqtu'wukpi 'V guv0' **Results:** Qh'574''uwdlgevu'*78' ''y qo gp.''o gcp"ci g'75'Õ'3507''{gctu.'83' ''y j kg.''44' ''drcem''7' '' J kır cpke+:''336'*54' +'y gtg''pqto qvgpukxg.''376'*66' +''r tg/j { r gtvgpukxg''cpf ''; 6'*46' +'' j { r gtvgpukxg0'Hqt''y g''r ctco gvgtu''cdqxg.''y gtg''pq''f kthgtgpegu''dgw ggp''y g''j { r gtvgpukxg'' i tqwr ''cpf ''j g''r tgj { r gtvgpukxg'' tqwr0''

"	DR"	I nwe"	LOOC"	J dC3E"	NF N"	JFN"	VI "	DO K	Y E"
	ooJi"	oilfN"	JUUU	' ''	o i lf N"	oilfN"	o i lf N'	mi lo ⁴ "	eo "
Data appulya"	224104"	; 50, "	40;"	707"	32:07"	8206"	;908"	4:04"	;605"
P qto qvgpuxxg	334194	Õ3809"	Õ408"	Õ208"	Õ4: 09"	Õ3902"	Õ72 ()"	Õ70 "	Õ3703"
Rtgj {rgtvgpukxg"	34: 1: 2"	32208" Õ'360, "	5097" Õ'50 "	709" Õ208"	33702" 'Õ' 5: 02"	7704" Õ'3508"	337 @ " Õ'8803"	5207" Õ707"	3240 " Õ'3603"
r "xcnwg"		2@23"	2@3"	2024''	2034"	2022; "	2@34"	2@228"	2@223"

I nxe'? 'i nxequg.'I QOC''? 'j qo gquxcvke''o qf gri'cuuguuo gpv.'I dC3E''? 'j go qi mdkp''C3E.'DOK? ''dqf { 'o cuu'kpf gz.'' Y E''? 'y ckuv'ektewo hgtgpeg0'

Conclusion: EXF 'tkumlhcevqtu'cr r gct''vq'enwuygt''kp''uwdlgewi'y ky ''r tgj {r gtvgpukqp.''r nekpi ''y gug'' uwdlgewi'cv'hpetgeugf ''tkumlhqt''EXF ''o wej ''hng''uwdlgewi'y ky 'j {r gtvgpukqp0''Kp''r ctvkewret.'' f {urkr kf go kc''cpf ''i nxequg''f {uo gvcdqrkuo ''eq/gzkuv'y ky ''xgt {''o qf guv'kpetgeugu'kp''DR.''nc {kpi ''c'' hqwpf cvkqp'hqt''o gvcdqrke''u{pf tqo g0'Kp''cr r n{kpi ''ewttgpv'DR''i wkf grkpgu'vq''y ku''r qr wncvkqp''qh'' r tgf qo kpcpvn{''o kf f ng/ci gf ''y qo gp.''uwdlgewi'y qwf ''dg''nghv'xwpgtcdng''cpf ''wptgeqi pk gf 'hqt''y gkt'' kpetgeugf ''tkun0'Uwej ''uwdlgewi''f gugtxg''emug''uetwkp{''hqt''y gkt''eqo qtdkf ''tkun1hcevqtu''cpf '' kpvgtxgpvkqpu'y ky ''vcti gygf ''rkhguv{ng''ej cpi gu0'

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...

Gpi ngt. 'TL 'Xgtpcrku'O P. 'O co wrc'MC. 'Drcendwtp''J N. 'Mcuj cpk'O. 'Gruy qtvj 'F N0''
 Nkr qr tqvgkp 'Kpuwrkp'Tgukuvcpeg''Kpf gz '*NR/KT+'Ej cpi gu'y kj 'Y gki j v'Nquu'Hqmqy kpi '3'[gct''
 Nqy 'Hcv'Xgi cp'F kgv0/American College of Cardiology, 64th Annual Scientific Session.'O ctej ''
 36/38.''4237.''Ucp''F kgi q.''EC0'

Cduxtcev"

Background<"Nkr qr tqvgkp"Kpuwkp"T gukucpeg"Kpf gz "*NR/KT +'ku'c'pqxgn'r tqr tkgvct { 'pqp/i gpf gt" ur gekhe 'ecnewicvkqp'hqt'kpuwkp'tgukucpeg'dcugf "qp"nkr qr tqvgkp'uwd/r ctvkeng'ukt g'f kuvtkdwkqp0"NR/ KT 'ku'f guetkdgf ''cu''c'tgncdng''dkqo ctngt 'hqt 'r tqi tguukqp''vq''f kcdgvgu''y cv'tghrgewi'ko r tqxgo gpwi'kp" o gvcdqnke''u{pf tqo g'hqmqy kpi 'f kgvct { htkguv{ ng'kpvgtxgpvkqpu'y kj 'y gki j v'nquu0"'' **Objective**<'Va''eqo r ctg'r guv/f kgvltkbguv{ ng'kpvgtxgpvkqpu'y i g'muv'y gki i y'cnf 'f get gcugf ''

Objective<'Vq''eqo r ctg''r quv/f kgvlnkhguv{ ng'kpvgtxgpvkqp''uwdlgevu''y j q''nquv'y gki j v'cpf ''f getgcugf '' xgtuwu''kpetgcugf ''y gkt ''NR/KT''kpf gz0''''

Methods<"Qxgty gki j vlqdgug'uwdlgewi'y kj 'ectf kqxcuewrct'f kugcug'*EXF +''qt'uki pkhecpv'EXF '' tkumihcevqtu''gptqmgf 'kp'c'3''{gct'kpvgpukxg'hkhguv{mg'kpvgtxgpvkqp'r tqi tco 'kpenwf kpi ''my 'hcv'*>32' +'' xgi cp''f kgv0Tkumihcevqtu.''cpyj tqr qo gytkeu''cpf ''dkqo ctmgtu'*kpenwf kpi ''NR/KT.'hkr kf ''r tqhkrgu.''gve0+'' cuuqekcvgf ''y kj ''EXF ''tkumi'y gtg''o gcuwtgf ''dghqtg''cpf ''3''{gct''chvgt'kpvgtxgpvkqp'hqt''eqo r ctkuqp''q'' y gki j v'muu''ej cpi gu0'''Uwdlgewu.''uvtcvkhkgf ''d{ ''NR/KT 'f getgcug''qt'kpetgcug''chvgt''3''{gct.''y gtg'' eqo r ctgf ''wukpi ''Y kreqzqp''pqpr ctco gytke''yguv0'''

Results<"O quv'r ctvlekr cpwl**p? 324.'6; 'o crgu.'75'hgo crgu+'eqo r rgvgf 'vj g'r tqi tco 'v kj 'v gki j $\sqrt{1000}$ rqud'Vy q'i tqwr u'y gtg'kf gpvkhlef ''d{ ''NR/KT''ej cpi g<"'NR/KT''ueqtg'kpetgcug'*471324?4607' +=''NR/KT''f getgcug'*991324?9707' +0''C v'dcugthpg.''vj gtg''y gtg''pq''uki pkhlecpv'f khtgt gpegu''dgw ggp''vj gug'' w q''NR/KT''i tqwr u''d{ ''ci g. 'DO K''u{uvqtle f kcuvqtle''DR.''J F NINF Nhqvctlej qrguvgtqrliqt''vtki n{egtkf gu'' dw'o gcp''NR/KT''ueqtgu''y gtg''uki pkhlecpvn{''f khtgt gpv'*r ?2023; +0''Ej cpi g''kp''J F N/E.''vtki n{egtkf gu.'' cpf ''NR/KT''ueqtg''chvgt''3''{gct''f khtgt gf ''uki pkhlecpvn{''f khtgt gpv'*r ?2023; +0''Ej cpi g''kp''J F N/E.''vtki n{egtkf gu.'' cpf ''NR/KT''ueqtg''chvgt''3''{gct''f khtgt gf ''uki pkhlecpvn{''f gwy ggp''i tqwr u'*r ?202376.''r ?202246''cpf'' r ?>20223.''tgur gevkxgn{+0'''

	LP-IR Increased (N=25)			LP-IR (Between Groups		
Bish Franks	Baseline	Year1	%	Baseline	Year 1	%	P-Value
RISKFactor	(SD)	(SD)	Change	(SD)	(SD)	Change	
PMI (kg/m2)	33.556	30.02	10 54%	33.82	30.561	0.64%	0.4425
Divir (kg/m2)	(7.715)	(7.409)	-10.3470	(6.73)	(6.225)	-3.0470	0.4455
Systelic PP (mm	124.16	126.56		127 142	100 1 00		
Systone BP (mm	(15 22)	(14 669)	-5.66%	(17.046)	(17 257)	-6.53%	0.7851
ng/	(15.22)	(14.005)		(17.545)	(17.557)		
HDL C (mg/dl)	48.32	43.96	c cook	44.532	43.688	1 00%	0.0154
HDE-C (mg/ di)	(11.131)	(9.176)	-9.02%	(13.5)	(11.679)	-1.50%	0.0154
	120.375	108	10.00%	109.613	106.133	7.179/	0.0555
LDL-C (mg/di)	(32.87)	(29.376)	-10.20%	(39.539)	(34.511)	-5.1770	0.0555
T. CUOL ((-41))	206.92	193.8	6.2.00	191.26	179.013	C 4004	0.7000
I-CHOL(mg/dl)	(39.841)	(38.636)	-6.34%	(46.04)	(41)	-6.40%	0.7088
TO ((-11)	183.08	206.6	40.059/	183.701	147.701	10.000	0.0004
IG (mg/dl)	(110.671)	(116.635)	12.85%	(91.098)	(78.629)	- 19.60%	0.0024
1.0.10	58.24	66.72	44.55%	71.662	55.714	00.0554	. 0001
LP-IK	(20.001)	(21.384)	14.56%	(16.126)	(18.773)	-22.25%	<u><.0001</u>

Conclusion "Vj g"o clqtk{ "qh'kpf kxkf wcnı'y j q'nqug'y gki j v'tgf weg''y gkt "NR/KT0"J qy gxgt."c" uwdi tqwr "*47' + "qh'r cvkgpvu'kpetgcugf "y gkt "NR/KT "f gur kg'y gki j v'nquu0"Vj g"enkpkecn'cpf " r tqi pquvke "uki pkhkecpeg"qh'y gug''qdugtxcvkqpu'tgs wktg'hwty gt "uwwf {0""

Abstract Submitted for Poster Presentations:"

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Mcuj cpk'O. 'Grkcuuqp'C.'Gpi ngt'T.'Vwtpgt'G.'Vuej knł 'P.'I twpgy cnf 'O.'J cnug{'L'Hwngt'E.''
 Xknłpgu'V. 'Xgtpcrku'O 0Rtgf kcdgvgu'Tgxgtucri/Wukpi 'c'P qxgrlEqo r tgj gpukxg'J gcnj 'O qf gn0'
 American College of Cardiology, 64th Annual Scientific Session.'O ctej '36/38.''4237.''Ucp''
 F kgi q. 'EC0'''

Cduxtcev"

Introduction: 'Qxgt'j chi'qhi'r tgf kcdgvleu'y knif gxgmr 'htcpnif kcdgvgu0Rtgf kcdgvgu'ku'c'o qf khcdrg" tkumihcevqt'hqt'ectf kqxcuewrct'f kugcug'*EXF +'y cttcpvkpi 'r tgxgpvkxg'kpvgtxgpvkqp0' Objective: 'Y g''gzco kpgf 'y g''ko r cev'qh'c'o wnkeqo r qpgpv'kpvgtxgpvkqp''qp''y g''EXF 'tkumi'r tqhkrg'' qh'uvdlgevu'y ky 'r tgf kcdgvgu'y j q''uveeguuhwm{ 'tgxgtugf 'y gkt'f kugcug'y kj qwi'go r j cuk kpi 'y gki j v' muu0'

Methods: 'Eqpugewkxg'uwdlgewl'qh'y g'Kpvgi tcvkxg'Ectf kce'J gcny 'Rtqlgev'Tgi knt {.'c'34/o qpy " EXF 'Tkun'Tgf wevkqp'Rtqi tco 'hqewukpi ''qp'hqwt'r knctu<'pwtkkqp."gzgtekug.''utguu'cpf ''urggr " ko r tqxgo gpv.''eqo r nyvgf ''xcrkf cvgf ''s wguvkqppcktgu'cpf ''y gtg''ecvgi qtkl gf ''cu''r tgf kcdgvke'''s nwequg'>'' 322''o i lf N''cpf '>''362''o i lf N+''qt'tgxgtvkpi ''r tgf kcdgvgu'*i nwequg'>''322''o i lf N+0'F kcdgvkeu'y gtg'' gzenwf gf 'htqo ''y g'cpcn{uku0'F khgtgpegu'y gtg''cpcn{| gf ''wukpi ''v vgu0'

Results: 'Qh'72: 'uwdlgevu'*78' 'y qo gp.''o gcp''ci g'75' \tilde{O} '3507''{gctu.''83' 'Y j kg.''44' 'Drcem''7' '' J kr cpke+.''329'*43' +'j cf 'r tgf kcdgvgu'y kj ''o gcp''J i C3E''70' '' cpf ''o gcp''i nvequg''32: 08''o i lf N0' Qh'r tgf kcdgvkeu.''74'*6; ' +'tgxgtvgf ''vq''pqto cn'i nvequg''gxgm0'

Risk Factor (n=52)	Baseline	6-month	p value
Hcuvkpi 'I nvequg'*o i If N+'	32706'Õ'804''	;406'Õ706''	>2@23"

Hcurkpi "Kpuwnkp"*wnWlo N+"	3607'Õ3208''	3206'Õ'905''	2024"
J qo gquvcvke'O qf gn'Cuuguuo gpv'	50 'Õ'409''	406'Õ'309''	20224"
Vqvcn'Ej qnguvgtqn'*o i 1f N+"	3; 2 0 9'Õ'630B''''	39703'Õ'5; O2''	2027"
Nqy 'F gpukv{ 'Nkr qr tqvgkp'*o i 1f N+''	3370 'Õ'5805''	32407'Õ'5609''	2028"
U{uvqnke "Dnqqf" Rtguuwtg'*oo" Ji+"	35605'Õ3707''	3490, 'Õ'3508''	2025"
DO K*mi lo ⁴ +"	52Œ'Õ7�"	4; 02'Õ70 "	2062"
Ogf kgttcpgcp"F kgv'S wguvkqppcktg"*36"r qkpw+"	80 'Õ'406''	;04'Õ'402''	20224"
Cgtqdke'Gzgtekug''Vkog''*okp1yggm+"	35806'Õ35; 08''	3; 40, 'Õ'38309''	2027"
Rgtegkxgf "Utguu"Uecng"*78"r qkpu+"	430, 'Õ'906''	3: 09'Õ'902''	2025"
Rkvudwti "Unggr "S workv{ "Kof gz "**43"r qkpvu+"	902'Õ'506''	709'Õ'509"	202: "
Hcvki wg"Uegtg"*32"r gkpvu+"	604'Õ'30, "	505'Õ4O2''	2025"

Conclusion: 'C "eqortgj gpukxg'j gcnj 'r tqitco "gorj cukļ kpi "eqodkpgf 'kortqxgogpuu'kp" pwtkskqp."gzgtekug."uvtguu'cpf 'unggr 'oc{'j gm 'uvdlgevu'y kj 'r tgfkcdgvgu'tgxgtv'vq''pqtocn'i nvequg" ogvcdqnkuo 'y kj qw'uvduvcpvkcn'ej cpi gu'kp'DOK/Eqodcvvkpi 'r tqitguukqp'vq'fkcdgvgu'y kj 'c" r tcevkecn'hklguv{mg'kpvgtxgpvkqp'nqygtu'EXF 'tkum'cpf 'kortqxgu'qxgtcm'jgcnj 'kp'vjku'xwpgtcdmg'' r qrwncvkqp0'

Abstract Submitted for Poster Presentations:"

Ä Mcuj cpk'O.'Grkcuuqp'C.'Gpi rgt'T.'Hwrgt'E.'Xkrrkpgu'V.'Xgtpcrku'O 0'O qf guv'Grgxcvkqp'kp" Drqqf 'Rtguuwtg'ku'c'Tgf 'Hrci 'hqt'Ectf kqxcuewrct'F kugcug'Tkur0/AHA Epi/Lifestyle 2015." O ctej '42370'

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"

Cduxtcev"

Introduction: 'E wttgpvn{."ectf kqxcuewrct 'f kugcug'*EXF +'tkum'o c{"dg"wpf gtguvko cvgf 'kp"uwdlgevu" y kj 'o qf guv'grgxcvkqp'kp'DR"cu'r tqxkf gtu"ctg"cf xkugf 'vq'hqewu"qp"'j g"vtgcvo gpv'qh'j {r gtvgpukqp" y j gp"o cpci kpi "drqqf 'r tguuwtg0"

Objective: "Y g'gzco kpgf ''y g'EXF 'tkuni'r tqhkg''qh'uwdlgewi'y kj ''o qf guv'DR''grgxcvkqp''q'' f gvgto kpg''y g''r tgxcrgpeg''qh'tkuni'rcevqtu''cpf ''q''kf gpvkh{ ''vcti gwi'hqt''kpvgtxgpvkqp0' **Methods:** Eqpugewikxg''uwdlgewi'gpvgtkpi ''y g''Kpvgi tcvkxg''Ectf kce''J gcnj ''Rtqlgev'Tgi knt { ''*c''34/ o qpvj ''EXF ''Tkuni'Tgf wevkqp''Rtqi tco +''y gtg''cuuguugf 'hqt''cpvj tqr qo gvtkeu''cpf ''c''EXF/tgrgxcpv'' rcd''r cpgf0'''Uvdlgewi'y gtg''ecvgi qtk gf ''cu''DR''pqv''grgxcvgf '*≥3421: 2+:'o qf guv'grgxcvkqp''kp''DR'' *@421: 2''cpf ''>3621; 2+''cpf ''j {r gtvgpukxg''*DR@621; 2+0''Eqo r ctkuqpu'y gtg''o cf g''dgw ggp'' uwdlgewi'y kj ''pq''DR''grgxcvkqp.''o qf guv'DR''grgxcvkqp''cpf ''j {r gtvgpukxgu''hqt''f khgtgpegu'kp''EXF '' tkuni'rcevqtu''wukpi ''vguv0'

Results: Qh'574'uwdlgewi^{**}78' 'y qo gp.''o gcp''ci g'75'Õ'3507''{gctu.'83' 'y j kg.''44' 'drcem'7' " J kır cpke+.''336'*54' +'j cf ''pq''grgxcvkqp''kp''DR.''376'*66' +'j cf ''o qf guv''grgxcvkqp''kp''DR''cpf '': 6'' *46' +'y gtg''j {r gt ygpukxg0'''''

BP	BP	Glucose	нома	HbA1C	LDL	HDL	TG	BMI	WC
Category	mmHg	mg/dL	ΠΟΜΑ	%	mg/dL	mg/dL	mg/dL	kg/m ²	cm
Not	224104"	; 50, "	40;"	707"	32:07"	8206"	; 908"	4:04"	;605"
Elevated	334194	Õ'3809''	Õ408"	Õ208''	Õ'4: 09''	Õ'3902"	Õ72 9 "	Õ70 "	Õ3708''
Modestly	24.1.2"	32208"	5097"	709"	33702"	7704"	33709"	5207"	3240 "
Elevated	54: I. Z	Õ'360, "	Õ'50 "	Õ208''	"Õ'5: Ø"	Õ'3508"	Õ'8803"	Õ707"	Õ3603"
p value	"	20223"	2023"	2024"	2084"	2022; "	2@34"	2@228"	2@223"

DR"? "dmqf "r tguuwtg."J QOC"? 'j qo gquvcvke"o qf gri'cuuguuo gpv."J dC3E"? 'j go qi mdkp"C3E. "DOK? "dqf {"o cuu" kpf gz."Y E"? 'y ckuv'ektewo hgtgpeg0'

Hqt''y g'r ctco gvgtu''cdqxg.''y gtg''y gtg''pq''f khlgtgpegu''dgw ggp''y g''j {r gtvgpukxg''i tqwr ''cpf ''y g'' i tqwr ''y ky ''o qf guv''grgxcvkqp''kp''DR0'

Conclusion: EXF 'tkuniheevqtu''cr r gct 'vq''dg'kpetgcugf 'kp''uwdlgewi'y kj 'o qf guv''grgxcvkqp''kp''DR." r reckpi ''j gug''uwdlgewi'cv''kpetgcugf 'tkunihqt''EXF ''o wej ''hkng''uwdlgewi'y kj ''j {r gt vgpukqp0'' Ur gekheem{.''f {urkr kf go kc.''i nwequg''f {uo gvcdqnkuo ''cpf ''qdgukx{ ''eq/gz kuv'y kj ''xgt {''o qf guv'' kpetgcugu''kp''DR.''rc {kpi ''c''nqwpf cvkqp''hqt''o gvcdqnke''u{pf tqo g0'Kp''cr r n{kpi ''evttgpv'DR''i wkf gnkpgu'' vq'yj ku''r qr wrcvkqp''qh''r tgf qo kpcpvn{ ''o kf f rg/ci gf 'y qo gp.''uwdlgewi'y qwrf ''dg''nghv''xwpgtcdrg''cpf '' wptgeqi pk gf ''nqt''yj gkt''kpetgcugf ''tkun0'Uwej ''uwdlgewi'f gugtxg''enqug''uetwkp{ ''hqt''yj gkt''eqo qtdkf '' tkuniheevqtu''cpf ''kpvgtxgpvkqpu''nqt''ci i tguukxg''o cpci go gpv0'

The following are key activities accomplished in the past year:

- A Uvtcvgi ke''r ncp''f gxgnqr gf ''vq''u{pej tqpl g''enkplecn'crrtqcej ''vq''eqortgj gpulxg''r tgxgpvlqp''cpf " EX''j gcnj ''d{ ''uvcpf ctf k kpi ''r tcevlegu''qh'5''KEJ R'P wtug''Rtcevlxkqpgtu''kp''kpvgtcevlpi ''y kj '' r cvlgpvu''cpf ''enkplecn'vgco 0'
- •ÁKEJ R"enkpkecn'i vkf gnkpgu'wrf cvgf 'vq't ghrgev'ncvguv'gxkf gpeg''qh'ectf kqxcuewnct'j gcnj 'r tcevkeg'kp'' r tgr ctcvkqp'hqt'kpkkcvkqp''qh'tgugctej 'r tqvqeqnu0'
- AF gxgnqr o gpv'cpf 'ko r ngo gpvcvkqp''qh'Gz gewkxg'O gf kekpg''Rtqi tco ''cv'tgs wguv'qh'QVUI <' EA Tgs wguv'htqo ''Qhhkeg''qh'yj g''Uwti gqp'I gpgtcn'*QVUI +'vq''ngctp''o qtg''cdqwv''REJ R''r tqi tco '' cpf ''ku''r qvgpvkcn'kp''ko r cevkpi ''yj g''j gcnyj ''cpf ''y gmpguu''qh'I gpgtcn'Qhhkegtu0'Kphqto cvkqpcn'' o ggvkpi ''y kj ''pwtkkkqpcn'hqqf ''f go qpuvtcvkqp''eqpf wevgf ''qp''34'B7'B5''y kj ''xgt { ''r qukkxg'' hggf dcem'htqo ''QVUI 0'
 - Ä Etgevkqp''qh'ewuvqo k gf 'r tqi tco ''q''cf f tguu'j genj ''qh'qwt ''pevkqpøu''ngef gtu0/Rtqi tco '' kpxqnxgf ''pwo gtqwu''o ggvkpi u'hqt''uvtevgi ke''r neppkpi ''epf 'f gxgnqr o gpv''qh''qwtgeej ''KV'' uqhwy etg''er r nkevkqp''hqt''eqngevkqp''qh'j genj ''uvtxg{u0''O wnkf kuekr nkpet{''uvchh''gzr gtvkug''wugf '' vq''etgevg''r gtuqpenk gf ''r nepu'qh''eetg.''deugf ''qp''y g''KEJ R'o qf gn''hqt''ur qwugu''qh''hqwt/wet'' i gpgteni''epf ''y g''Cto {''Uwti gqp''I gpgten'*VUI +0'
 - EAJ ki j n{ 'uweeguuhwn'gxgpv'*O ctej '6. '4236+'gzgewgf ''cv'yj g''VUI øu'j qo g''cv'HoO eP ckt'' eqpf weykpi ''cp'kpygtcevkxg'J gcnj { ''Nkxlpi ''Y qtmj qr ''ewuvqo k gf 'hqt''ngcf gtu'kp'j ki j n{ '' uvtguugf ''qeewr cykqpu0'VUI ''j cu'tgs wguvgf ''vq''eqmcdqtcvg'hwtyj gt''y kj ''yj g''KEJ R''vgco ''dcugf '' qp''y g''uweeguu''qh'yj g'O ctej ''gxgpv0'
 - $\stackrel{\text{''}}{=} \stackrel{\text{''}}{=} \stackrel{''}}{=} \stackrel{''}}{=} \stackrel{''}}{=} \stackrel{''}}{=} \stackrel{''}}{=} \stackrel{''}}{=} \stackrel{''$
- A KEJ R'F cvcdcug"cpf "Rrcvhqto "Etgcvkqp"eqpvkpvvgf <"

- ËÁ Rtqxkf gt 'ur gekhe'o ggvkpi u'y kj 'KV''ur gekonkuvu''eqpf wevgf 'hqt 'enkpkeon'hggf doem'
- EA Htqpv'f gumir tqeguu'cpf 'hqy 'f gxgqr gf '\q'f qxgvckiy kj 'enkpkecn'o krguvqpgu0Tgxkgy 'cpf '' tghkpgo gpv'qh'r tgxkqwu'gf kw'eqo r ngvgf 'kp''cpvkekr cvkqp''qh'dgvc''vguvkpi 'r tqlgevgf 'hqt'' P qxgo dgt0'
- ÄHtqpv'gpf/uwtxg{"o gej cpkuo "dwkn/y ky "enkpkecn'gpf "r gpf kpi "vguvkpi 0"
- •Á F cvc'O cpci go gpv'Rncp'kp'r tqi tguu'y kj 'o gti kpi 'qh'f cvc'htqo 'vy q'r tgxkqwu'f cvcdcugu'kp'' qtf gt'vq'o qxg'hqty ctf 'y kj ''qpg'f cvcugv'hqt 'hwtyj gt''cpcn{uku0'''
- A Wrfcvgf 'vj g'uvcpfctfk gf 'crrtqcej 'vq 'Ectqvkf 'Kpvko cn'O gf kc''Vj kempguu'o gcuwtgo gpv'cpf '' kpvgtrtgvcvkqp 'hqt'tgugctej 'rtqvqeqnu'y kj 'wktk cvkqp 'qh'pgy 'gs vkr o gpv0'
- •Á Uvcpf ctf k gf 'Eqcej kpi 'Ecm'Rtqeguu'tghkpgf 'cpf 'ko r no gpvgf 'vq''gpeqwtci g''cfj gtgpeg''q'' nthguv{ ng''ej cpi gu'kp''qtf gt 'vq''o ckpvckp'i ckpu0'
- •Á KEJ R'Utguu'O cpci go gpv'EF 'kp'f gxgnqr o gpv'hqt'r tqf vevkqp'd{ 'Ft0I qtf qp'kp'Y TPOOEøu'' dgj cxkqtcn'j gcnj 'ugtxkeg'vq'kpenxf g'vtcemk/3+'Tkug'vq'c'P gy 'Fc{''4+'Vgpukqp'Vco gt''5+'Rqy gt''

Fqyp'hqt'Tguvhwn'Unggr0'

- ■Á KEJ R'dcugf ''eqi pkkxg''dgj cxkqtcn'yj gtcr { ''*EDV+'kpvgtxgpvkqp''hqt''kpuqo pkc''wktk kpi ''EOG'' f gxgrqr gf ''cpf ''uwdo kwgf ''hqt''Y TPOOE''KTD'tgxkgy 0'
- •Á Cf qr vkqp''qh''KEJ Røu''Nkhguv{ng''Rtguetkr vkqpu''d{''y g'Cto {''Uwti gqp'I gpgtcn'*VUI +'hqt''DI '' Enctnøu''Tgukrkgpe{''ghhqtwi'cv'Y TPOOE0KEJ R'ku'j qpqtgf ''vq''r tqxkf g''y ku'ugtxkeg0'
- •A Eqncdqtcvkxg"ghqtvu'vq"gzrcpf 'uekgpvkhke'o qrgewrct 'y qtmiy ky "enkpkecn'egpvgtu''qh'gzegrrgpeg0'
- A Hwwtg'r tqvqeqnu'vq go r j cult g'wplthgf "ÆJ R"crrtqcej "vq"eqo dcv'EXF. "eqi pkkxg'f gentpg"cpf " ecpegt0'

<u>Sub Task #3.1 Continuation of the "Validation of the ICHP Cardiovascular Risk Score"</u> protocol.

<u>Ogyiqfqmqi</u>{"

F cvc'r tgxkqwuf 'eqngevgf 'qp'r cvlgpu'gptqngf 'kp''y g'Rtqur gevkxg'Cto { 'Eqtqpct { 'Ecnekvo '' *RCEE+'cpf 'RCEE 'T guecp'r tqlgewi'y gtg'tgxkgy gf 0'Ur gekke 'kphqto cvkqp'y cu'i cy gtgf 'cpf '' cpcn{| gf ''q'i kxg"gcej 'r cvkgpv'c'EX'f kugcug'tkmiueqtg'ceeqtf kpi ''q'c'hqto wrc'f gxgrqr gf 'd{ ''y g'' KEJ R0'Vj ku'KEJ R'hqto wrc'wugu'y g'Htco kpi j co 'o qf gri'qh'tkmi'r tgf kevkqp''cpf ''cff u'j kurqtecn' hcevqtu'cpf ''dkqej go kecn'o ctngtu''q''r tqf weg'c'pqxgriueqtg'r tgf kevkg''qh'EX'f kugcug'tkmi'kp'' o kfxct { ''dgpghkekctkgu0'Vj g'i qcn'qh'yi g''uwf { ''y cu''q''xcrlf cvg''y g''wkrks{ ''qh'y ku''pqxgri'KEJ R'ueqtkpi '' u{uvgo ''d{ ''eqo r ctkpi ''y g'' tgf kevgf 'tkmiy kj ''qweqo gu'kp''y ku'y gn'ej ctcevgtk gf ''r qr wrcvkqp0'Vj g'' r tko ct { ''qdlgevkxg"qh'y g'' tqlgev'y cu''q''xcrlf cvg''y g'' tgf kevkg''wkrks{ ''cpf ''ceewtce{ ''qh'y g''KEJ R'' EX'tkmiueqtg'*'qt''KEJ R'ueqtg+0'Ur gekhecm{ .''y g'' qcm<c'-t''q''f gvgto kpg'kh'y g''KEJ R''ueqtg'' eqttgrevgu'y kj ''etquu/ugevkqpcni' tgxcrgpeg''qh'eqtqpct { ''ecrekvo ''cu'o gcuvtgf ''kp'y g''RCEE''r tqlgev''' cpf ''d+'y kj ''y g''f gxgrqr o gpv'qh'EJ F ''gxgpvu'uvej ''cu''cpi kpc.''o { qectf kcnlkphctevkqp.''qt''pggf ''hqt'' EX'kpvgtxgpvkqp'uwej ''cu''eqtqpct { ''uvgpvkpi .''cpi kqr rruv{ .''qt''d {r cuu'uvti gt {0'C ''y kff '' qcn''e+''q'' f gvgto kpg''y g''eqttgrcvkqp''qh''y g''KEJ R''ueqtg''y kj ''eqtqpct { ''ecrekvo ''r tqi tguukqp''cu'o gcuvtgf ''kp'' g''g''RCEE'tguecp''r tqlgev0'

Mg{ "Hkpf kpi u1Eqpenwukqpu<"

 $\label{eq:main_star} \begin{array}{l} Mg \{ "hwf { hpf hpi u'y gtg'o quv'tgegpvn { 'tgr qtvgf 'hp''y g''Y : 3ZY J /33/4/2449" { H[34/36'[t''3+" Cppvcn'Tgr qtv'f cvgf 'Qevqdgt''49.''42340' \\ \end{array}$

Status:

Manuscripts Published (See Appendix A):

• Á Mcuj cpk'O. 'Grkcuuqp'C. 'Dckrg{'M 'Xgtpcrku'O 0'C 'u{uvgo cvke''crrtqcej 'kpeqtrqtcvkpi 'hco kn{" j kuvqt{'kortqxgu'kf gpvkhkecvkqp''qh'ectfkqxcuewrct'f kugcug'tkun0'J of Cardiovasc Nurs0'4236'' O c{ ''420']Gr wd''cj gcf ''qh''r tkpv_'''

The following are key activities accomplished during the past year:

- •ÁKEJ R'Enkplecn'F gekukqp''Uwr r qtv''Vqqn'cevkxgn{"cr r nkgf '\q''enkplecn'gpeqwpvgtu'\q'ko r tqxg''EXF " tkum'encuukhlecvkqp0'
- •Ákþenvukqp"qh"pgy "ectf kqxcuewrct"tkumueqtkpi "u{uvgo u'*kkg032/{gct"tkum"cpf"nkhgvko g"tkum#kp"qwt" enkpkecn"o qf gn"i kxgp"yj g"i wkf cpeg"htqo "yj g"Co gtkecp"Eqmgi g"qh"Ectf kqnqi {"Eqphgtgpeg" 42360"
- •ÁKor ngo gpvgf ''y g''KEJ R'Enkpleen'F gekulap''Uwrrqtv''Vqqn'wugf 'kp''enkpleen'gpeqwpvgtu''a''kortqxg'' EXF ''tkum'encuulkheevlap0'
- •ÁCpcn{uku'qh'f cvc'\q'hqqm'cv'f getgcukpi 'EXF "cpf 'kpetgcukpi 'ugnh'ghhkece { 'ueqtgu'hqt''

rwdnkecvkqp0

•Ákþkkcvkxgu'vq''ecr wtg''ÆJ Røu'ko r cev'qp''j gcnj "*improvement*''cu'y gm'cu'EXF 'tkum'tgf wevkqp<' S wcpvkscvkxg''cr r tqcej gu'vq''NKHG''Ueqtg'*Nkhg'Ko r cev'hqt'Go r qy gto gpv+''

<u>Sub Task #3.2: Initiate the "ZENITH (randomiZed Evaluation of a Novel comprehensIve</u> prevention program on aTHerosclerosis progression) Trial".

<u>Ogyiqfqmqi {</u>"

Vjg"r wtr qug"qh'yjku"qpg/{gct."rtqur gevkxg."tcpf qok gf."eqpvtqngf."kpvgtxgpvkqpcn'vtkcn"ku'vq" kpxguvki cvg''y g''ko r cev''qh''KEJ R/ERR''qp''xcuewrct''j gcnyj .''cvj gtquengtquku'r tqi tguukqp''cpf ''nghv xgpvt/sewrct"tgrczcvkqp"*f kcuvqrke"hwpevkqp+"co qpi "r cvkgpvu"y kj "kpetgcugf "hklgvko g"EXF "tkum"dw" ny "uj qtv'vgto "eqtqpct { "j gctv'f kugcug" *EJ F + "tkum" ceeqtf kpi "vq vj g"Htco kpi j co "Tkum" Ueqtg." HTU+"cu"eqo r ctgf "\q"tgegkxkpi "wuwcn"ectg" *WE+0Wr "\q"392"o crg"cpf "hgo crg"r cvkgpvu"dgw ggp"3: / 72"{ gctu'qh'ci g'y ky 'my ">32' +'32/{ gct'HTU'hqt'EJ F 'dw'guvko cvgf 'httgvko g'tkum'*q'ci g'; 7" {gctu+"qh"eqtqpct{"f gcyi "qt"o {qectf kcn"kphctevkqp"*O K+"qh'×"5; ' 'y kj qw"enkpkecm{"o cpkhguv" EXF "OK'eqtqpct { "qt'r gtkr j gtcn'ctvgtkcn'tgxcuewrctk cvkqp. "qduvtwevkxg"eqtqpct { "ctvgt { "f kugcug" *ECF+" gctv'hcknxtg" qt"egtgdtqxcuewrct" gxgpv_'y km'dg" tcpf qo kt gf "vq"r ctvkekr cvkqp" kp" y g" ewttgpvn{"qpi qkpi "KEJ R/ERR"qt"\q"WE0Vj g"rtko ct{"gpfrqkpv'ku"dgw ggp/i tqwr "fkhgtgpegu"kp" y g'ej cpi g'kp'xcuewrct "gpf qy grkchhwpevkqp"cu'o gcuwtgf "wukpi "F VO."cu'tgr qt vgf "cu'cf lwuvgf 0" Ugeqpf ct { "gpf r qkpvu"ctg"ej cpi gu"kp"o gcuvtgu"hqt "EKO V. "ectf kce"f kcuvqrke "hvpevkqp. "rkhgvko g" EJ F "tkumlueqtgu."cpf "y g"KEJ R'EX "Tkuml'Ueqtg0Kk'ku"j {r qvj guk gf "vj cv'r cvkgpvu"y kj "rqy/uj qtv" vgto "*Htco kpi j co "32/ {gct"EJ F "tkumueqtg+"dwv"j ki j "http://dwv qt'O Ky j q'r ctvlekr cvg'kp''y g''KEJ R/ERR''y kniko r tqxg''xcuewrct''j gcny "cpf ''tgf weg''cvj gtquengtquku" rtqi tguukqp"y j gp"eqo r ctgf "\q"y qug"tgegkxkpi "wuwcnlectg0"

<u>Status:</u>

Cppwcn'ET lcf f gpf wo 'lwdo kwgf '\q'Y TP O O E 'KTD'qp'52'Qev'35'cpf 'cr r tqxcntgeglxgf '9'Lcp'' 4236=hqty ctf gf '\q'J TRQ0Cf f gpf wo ''wr f cvgu'tgetwko gpv'o cvgtkcn. 'ecug'tgr qtv'hqto u.''ej cpi g'' kp'\go r qtct { ''ugtwo 'lwqtci g''nqeckqp''cv'Y TP O O E ''cpf ''ugxgtcn'gf ku'\q'kpxguvki cvqt'kphqto cvkqp0' Y TKr tqvqeqn'lwdo kwgf ''q'Ej gucr gcng''KTD''qp'8'O ct'36=f gvgto kpcvkqp''y cu'o cf g''y cv'y ku'' uwwf { 'ku'pqp/j wo cp''uwdlgev'tgugctej ''cv'Y TK0Tgr mego gpv'ectqvkf ''wntcuqwpf ''gs vkr o gpv'y cu'' tgeglxgf ''cpf ''tclpkpi ''eqo r ngvgf 0Eqngevkqp''qh''gej qectf kqi tco ''ko ci gu''tguqnxgf ''cpf ''eqngevkqp'' r tqvqeqn'lw'r meg0'Vtcpuhgt ''cpf ''ctej kxkpi ''qh''gej qectf kqi tco ''ko ci gu''tguqnxgf ''g' lhpcn'uvci gu'' qh'tguqnwkqp=''cevkxgn{ ''y qtnkpi ''y kj ''Y TP O O E 'Endplecn'Kphqto cvkeu''F gr ctvo gpv'\q'tguqnxg0' Tgetvkko gpv'eqo o gpegf ''gctn{ ''Lwn{ 0T getvkko gpv'j cu''dggp''uny =r mp''uvdo kuukqp''qh''r tqvqeqn'' cf f gpf wo ''y kj ''pgz v'ET '\q''gz ygpf 'tgetvkko gpv'r mp'\q'r wdne''ur cegu''cpf ''cf f kkqpcn'Y TP O O E '' enkplecn''ctgcu0'Gki j v'r cvkgpwi'j cxg''dggp''uetggpgf '\q'f cvg=5''o ggv'etkgtkc'\q''gptqm ''dw''cm'y cpvgf '' r tvkekr cvkqp'kp''pqp/uwf { ''KEJ R/EJ R'r tqi tco 0'

<u>Sub Task #3.3: Initiate the "Cardiovascular Prevention Program (CPP) Registry for the</u> <u>Integrative Cardiac Health Project" protocol.</u>

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Vj g'r wtr qug''qh'y ku'uwf { 'ku'\q''guvcdnkuj 'c'tgi kut { '\q''gpcdng'tgugctej ''qp'r cvkgpvu'cv'tkumhqt'' ectf kqxcuewrct 'f kugcug'*EXF +0''Cm'enkpkecm{ 'f gtkxgf 'r cvkgpv/tgrcvgf 'f cvc'hqt'uwdlgevu'' r ctvkekr cvkpi 'kp'y g'Y TPOOE''EJ R'y km'dg''gpvgtgf 'kpvq''c''ukpi ng.''ugewtg'f cvcdcug0'Cv'r gtkqf kecn' kpvgtxcnu.''cuuguuo gpv'qh'yj g''tgi kut { 'f cvcdcug'y km'emqy ''s vgtkgu''q''f ghkpg''yj g'ko r cev'qh''cp'' kpvgi tcvkxg'hkguv{ng''ej cpi g''r tqi tco ''qp''EXF 'tkum'qxgt''ko g0'Vj g'KEJ R'Tgi kut { 'y km'wkrkt g''y g'' KEJ R'f cvcdcug'y j kej 'f qewo gpvu'f go qi tcr j keu. 'tgur qpugu'vq'xcnkf cvgf 'nkhguv{ng'j cdku'' s wguvkqppcktgu'tgi ctf kpi "gzgtekug. 'f kgv.''uvtguu'cpf ''unggr .'r j {ukecn'gzco kpcvkqp"cpf '' cpvj tqr qo gvtkeu. 'ncdqtcvqt { ''yguv'tguvunu. 'ko ci kpi . ''cevki tcr j ke'f cvc. ''enkplecn'tgeqo o gpf cvkqpu''cpf '' eqpuvuncvkqpu. 'r ctvkekr cpv'o cpci go gpv.''cpf ''r ctvkekr cpv'xkuku0''

Rcvkgpwl'y km'dg"qhtgtgf "gptqmo gpv'kpvq"y ku'uwf {"cv'y g'vko g"qh'r tgugpvcvkqp"kh'y g{"ctg"o krksct {" j gcnj "ectg"dgpghkekctkgu"cpf "ctg"cv'rgcuv'3: "{gctu"qh'ci g0Cm'r ctvkekr cpvu."tgi ctf rguu"qh' gptqmo gpv'kp"y g'uwf {."y km'tgegkxg"y g'wuwcn'uvcpf ctf "qh"ectg"d{"y gkt"j gcnj "ectg"r tqxkf gtu0' Eqnrgevkqp"qh'o gf kecn'kphtto cvkqp"qp"KEJ R"uwdlgewl'ku'ceeqo r rkuj gf "y tqwi j "kpvgtxkgy "qh" r cvkgpwl'cu'y gm'cu'y tqwi j "tgxkgy "qh'o gf kecn'kphtto cvkqp"htqo "qy gt"hcekrkkgu'r tqxkf kpi "ectg0' Enkplecn'f cvc"eqnrgevkqp"qeewtu'cv'dcugrkpg"cpf "cv'y g"eqpenvukqp"qh'y g'kpvgtxgpvkqp."v{r kecm{"cv'8" o qpy u0Cf f kkqpcn'hqmy "wr "hqt 'uwr r qtv'qh'y g'r cvkgpvøl'i ckpu"cpf "cf f kkqpcn'f cvc"eqnrgevkqp" qeewt"cv'34"o qpy u"cpf "cppvcm{"hqt 'wr "\q"7"{gctu0Vj g'tgugctej "eqo r qpgpv'qh'y ku'uwf {"y km" kpxqrxg'y g"cpcn{uku'qh'enkplecn'f cvc"eqnrgevgf "cv'y gug"kpvgtxcn0"

Vj g"KEJ R"enkpleenif evedeug"eep"dg"s wgtkgf "cv'c"ukpi ng"ukwkpi "y kj "tgo qxen'qh"emi'r gtuqpem{ " kf gpvkh{kpi "kphto evkqp"vq"r gthqto "cuuguuo gpwl"qh"r tgxengpeg"qh"tkum. "cuuqekevkqpu"qh"dgj exkqtu" epf "tkum. "cpf "y g"uweeguu"qh"xetkqwu"kpvgtxgpvkqpu"qxgt"vko g0"Uvej "s wgtkgu"veng"o kpwgu"vq" r gthqto "cpf "eep"dg"eeeqo r nkuj gf "y kj "o kpko en'tkumivq"kpf kxkf wen'r tkxee{0Vj gtg"ku"pq"pggf "vq" o ekpvekp"ep{ "hpmei g"f eve"cu"vj g"kphqto evkqp"ku"j etxguvgf "ev'e"ukpi ng"ukwkpi "htqo "qpg"f evedeug"

Status:

Rtqvqeqn'crrtqxgf 'd{ 'Y TPOOE''KTD''qp''49''Oct''35='J TRQ''crrtqxgf ''qp''35'Pqx''350' Y TPOOE'ET ko gpfo gpv'crrtqxgf ''qp''49''Oct''36=''co gpfo gpv'wrfcvgu''uwtxg{ ''vqqn''ewttgpvn{" dgkpi ''wugf ''kEJ R'EJ R0Tgetwkso gpv'fgm{gf ''vpvkn'kpkkcn'KEJ R'fcvcdcug''yguvkpi ''ku''eqorngvg0' Cp''cffgpf wo ''vq''hwtyjgt''emtkh{ ''hqmqy / wr ''rqtvkqp''qh''yjg''KEJ R'hkguv{m''rtqitco ''ku''rmppgf ''pgzv'' s wctvgt0'

Sub Task #3.4 Collaboration on "Assessing Risk Factors for Cardiovascular Disease in Individuals with Traumatic Amputations" protocol (PI: Alison Pruziner), DPT, ATC, WRNMMC Dept of Rehab).

<u>O gyj qf qnqi { < "</u>

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Vj g''qdlgevkxg''qh'y ku''eqo r ctcvkxg''eqj qtv'uwaf {'ku''q''cuuguu''r tgugpeg''qh''mpqy p'tkunihcevqtu'hqt''EXF " kp'kpf kxkf wcni'y kj ''tcwo cvke''co r wcvkqpu0''Wr ''q'627'r ctvkekr cpui'y knidg''gptqngf ''cpf ''f kxkf gf ''kpvq'' y tgg''i tqwr upy l'plwt {.''tcwo cvke''co r wcvkqpu0''Wr ''q'627'r ctvkekr cpui'y knidg''gptqngf ''cpf ''f kxkf gf ''kpvq'' co r wcvkqp0F cvc'y knidg''eqngevgf ''cv'y q''vlo g''r qkpu. ''cv''vlo g''qh'eqpugpv''cpf ''cv''c''7/{gct''nqmy/wr '' xkukv''cpf ''y knihpenwf g'f go qi tcr j ke ''kpenwf kpi ''f kci pquku''qh'j {r gtvgpulqp.''j {r gtrkr kf go kc''qt''f kcdgvgu'' o gnkwu+''cpf ''hco kn{''j knqt {.''cpyi tqr qo gtke ''*j gki j v.'y gki j v.'y ckuv'ektewo hgtgpeg.''j kr ''ektewo hgtgpeg'' cpf ''dqf { ''eqo r qukkqp+.''dkqej go kecn'*ikr kf u 'hcurkpi ''dnqf ''uwi ct.''j go qi mdkp''C_{3e}.''hcurkpi ''kpuwkp.'' wntc/ugpukkxg'E''/'tgcevkxg''r tqvgkp.''hr qr tqvgkp'*c+''yj {tqkf ''uvlo wrcvkpi ''j qto qpg.''xkco kp'F.''cpf '' hdtlp'F /f ko gt+.''dnqf ''r tguuvtg.''j gctv'tcvg.''r wng''r tguuvtg.''GMI .''ectqvkf ''kpvko c/o gf kcn'y kemguu'' *'EKO V+'uwaf {.''uvtguu''cpf ''uggr ''uvtxg{u ''f kgv'*htvkv'cpf ''xgi gvcdrg'kpvcng.''qvcnhcv'cpf ''uvtcvgf ''hcv'' kpvcng+''uo qmkpi ''j kurqt { ''cpf ''cevkxks{ ''o gcuvtgu0/EXF ''tkurn'y kn'dg''guvko cvgf ''wukpi ''y g''ffygi tcvgf '' Ectf kce''J gcnj ''Rtqlgev'*KEJ R+'tkurn'cuuguuo gpv'cpf ''y g''P cvkqpcn''J gctv'Nwpi ''cfp ''Dnqf ''Kpukwwg'' *'P J NDK+'32/{gct'tkurn'guvko cvg0'K/ku'j { r qy guk g'y cvc'3+'Kpf kxkf wcn'y kj ''tcwo cvke''co r wcvkqpu'*C+'' y knij cxg'j ki j gt'ngxgnu'qh'hœvqtu''y cv'kpetgcug'tkum'šcpyi tqr qo gvt {.''dkqej go kecn'o ctngtu.''dnqf " r tguuwtg.''r wng''r tguuwtg. ''E KO V.''uvtguu.''r qqt''unggr ''j cdku. ''ucwtcvgf 'hcv'kpvcng.''uo qnkpi +''cpf ''nqy gt " ngxgnu'qh'hœvqtu'y cv'f getgcug'tkum'šhtwki'cpf ''xgi gvcdng'kpvcng''cpf ''cevkxk{+'hqt''EXF ''y j gp''eqo r ctgf '' q'kpf kxkf wcni'y kj qw''qtyj qr gf ke'kplwtkgu''*P +.''cpf ''y cv'y ku'tkun'y kn'eqpvkpwg''q'kpetgcug''qxgt''y g''7/ {gct'hqmqy /wr ='4+'Kpf kxkf wcni'y kj ''tcwo cvke''co r wcvkqpu'*C+'y kn'enq''j cxg''y g''uco g''kpetgcug' t'kum' hœvqtu.''cu''uvcvgf ''cdqxg.''y j gp''eqo r ctgf ''q''kpf kxkf wcni'y kj ''tcwo cvke''qty qr gf ke''kplwtkgu'y cv'f kf ''pqv'' tguwn'kp''co r wcvkqp'*Q+.''cpf ''ci ckp''y ku''tkum'y km'eqpvkpwg''q'kpetgcug''qxgt''y g''7/ {gct'hqmqy /wr .''cpf ='' 5+'Vj gtg'y kn'dg'pq'f khtgtgpeg'kp''r tgugpeg'qh'tkum'hœvqtu''dgw ggp'kpf kxkf wcni'y kj ''*Q+''cpf ''y kj qw'' qty qr gf ke'kplwtkgu'*P +.''y cv'f kf ''pqv'tguwn'kp''co r wcvkqp0'

Status:

Vqvcnluwf {"gptqmo gpv? 74"*46"eqpvtqm."47"co r wggu. '5"ko d"ucnxci g+<6"pgy "r cvlgpvu"gptqmgf "kp" r cuv"{gct0Gptqmo gpvf gm {u"ctg"f wg"vq"ko kgf "tgetvkso gpv"uwr r qtv"hqt"RK"kpcdkts/{ "vq" r gthqto " ectqvkf "wntcuqwpf "cpf "r mpu"vq"eqmgev"ugtwo "hqt"dkqo qngewnct"y qtm0Cf f gpf wo "uvdo kwgf "vq" Y TP O O E 'F TR"qp"33"Qev'35 'hqt"eqmgevlqp "qh"cf f kkqpcn"dmqf "uco r ngu"hqt"o qngewnct"cpcn{uku" cmpi 'y kj "RKej cpi g"vq"F t0Crkuqp"Nkpdgti "cr r tqxgf "qp"32"Hgd"36="cr r tqxgf" 'd{ "WUCO TO E " QTR"qp"36'Cr t "360C"tgegpv"co gpf o gpv"hqt"RKpco g"ej cpi g"htqo "Nkpdgti "vq"Rtw| kpgt"cpf" ej cpi g"kp"r tqeguukpi "qh'O CR"dkqo ctngt "uco r ng"uvdo kwgf "vq"Y TP O O E "F TR"cr r tqxgf "Lwn{" 4: ...4236="hqty ctf gf "vq"O TO E 'QTR0'Ucchi'kf gpvkhkgf "htqo "F gr ctvo gpv"qh"Tgj cdktkcvkqp"vq"cuuknv" kp"r cvkgpv"tgetvkso gpv"cpf 'r tqeguukpi "qh"dmqf "uco r ng"hqt"dkqo qngewnct"y qtn0'Vtckpkpi "y cu" eqpf wevgf "kp"Y TP O O E "Dkqo qngewnct 'Tgugctej "Ncd"*DTN+"kp"eqmcdqtcvkqp"y kj "Y kpf dgt" Tgugctej "Kpuvkwwg"qp"r tqeguukpi "qh'y gug"dmqf "uco r ngu0/#

Task #4: Follow-up data analysis and publications for the following protocols at WRI: 1) Global Profiling of Gene/Protein Expression and Single Nucleotide Polymorphisms Associated with Coronary Heart Disease Reversal and the Sub-Study for Subjects in the Dr. Dean Ornish Program and 2) Cardiovascular Risk Assessment and Prevention Program through the Cardiovascular Risk Clinic (CRC).

<u>O gyi qf qrqi {</u>"

Hqmqy /wr 'f cvc''cpcn{uku''cpf ''r wdrkecvkqpu'hqt''y g'hqmqy kpi ''r tqvqeqni'cv''Y TK' 3+'I mdcn'Rtqhkrkpi ''qh'I gpglRtqvgkp''Gzr tguukqp''cpf ''Ukpi ng''P wengqvkf g''Rqn{o qtr j kuo u'' Cuuqekcvgf 'y kj 'Eqtqpct{''J gctv'F kugcug'T gxgtucn'cpf ''y g''Uwd/Uwrf {''hqt''Uwdlgewu'kp''y g''F t0' F gcp''Qtpkuj ''Rtqi tco ''cpf ''4+'Ectf kqxcuewrct 'Tkum'Cuuguuo gpv'cpf ''Rtgxgpvkqp''Rtqi tco ''y tqwi j '' y g''Ectf kqxcuewrct 'Tkum'Erkpke''*ETE+0/Cnj qwi j ''gptqmo gpv'kp''y gug'r tqi tco u'ku'eqo r ngy.''y g'' y kn'eqpvkpwg''q'hkpcrk g'f cvc''eqnrgevkqp''cu''y gm'cu''eqpf wev'f cvc''cpcn{uku''qp''dkqej go kecn'o ctngtu.'' i gpg''gzr tguukqp''cpf 'UP R'f cvc.''cpf ''RGVIEV'ko ci kpi ''uwrf kgu''cpf ''y km'r tgr ctg'tguwnu'hqt'' r wdrkecvkqp0'

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1) Global Profiling of Gene/Protein Expression and Single Nucleotide Polymorphisms Associated with Coronary Heart Disease Reversal and the Sub-Study for Subjects in the Dr. Dean Ornish Program

1a) Ornish Program

<u>Status</u>:

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Gptqmo gpv'kpvq''y g'Ft0Fgcp''Qtpkuj 'Rtqitco 'ku'enqugf 'cpf 'cm'cevkxg'rctvkekrcpvu'j cxg'' eqorngvgf ''y gkt''rctvkekrcvkqp''kp''y g''uwwf{0Fcvc''cpcn{uku'ku''qpi qkpi 0'''

<u>Uwdlgev'Gptqmo gpv'cpf 'F go qi tcr j keu</u>"

Vj g'Qtpkij ''r tqi tco 'ku'emugf ''\q''gptqmo gpv'cpf ''cm'cevkxg''uwdlgewi'j cxg''eqo r myf ''y g''r tqi tco 0' Uwdlgev'gptqmo gpv'y cu'644''r ctvkekr cpvu'kpenwf kpi ''47''eqj qtvu''cpf '6'tgvtgcvu0'55; ''r ctvkekr cpvu'' i tcf wcvgf 'htqo ''y g''r tqi tco ''cpf '': 5''r ctvkekr cpvu''f kueqpvkpwgf ''r ctvkekr cvkqp'*42' ''f tqr qw'tcvg+0' F go qi tcr j ke''ej ctcevgtkuvkeu''qh''r ctvkekr cpvu'y gtg<'cxgtci g''ci g''qh'880B''{gctu.'75' ''hgo cmg.''55' '' xgvgtcpu''qt''y g''ur qwug''qh'c'xgvgtcp.''cpf ''63' ''j cf 'f kci pqugf ''eqtqpct {''j gctv'f kugcug0'''

Qweqo g'Fcc"

Rctvkekr cpwi'kp''y g'F t0F gcp''Qtpkuj 'Rtqi tco ''cv'Y kpf dgt''O gf kecn'Egpvgt''cej kgxgf ''uki pkhkecpv'' ko r tqxgo gpv'kp''gxgnu'qh'xkt wcm{ ''cm'qh''y g''o gcuwtgf "eqtqpct { ''ctvgt { ''f kugcug'*ECF +'tkumihcevqtu'' qxgt''y g''kpkkcn'34/y ggni'r gtkqf 0'O gcuwtgu''qh''qdgukv{ ''kpenvf kpi ''y gki j v'cpf 'DO Kf genkpgf ''¢9' ...'' rgxgnu''qh''qvcn'ej qnguvgtqn'y gtg''tgf wegf ''d { ''pgctn{ ''35' ...'dnqqf ''r tguuwtg''f tqr r gf ''¢; '...''o gcuwtgu'' qh''r j {ukecn'hkpguu'kpetgcugf ''o qtg''y cp''48' ...'cpf ''pxgnu''qh'f gr tguukqp''f getgcugf ''cr r tqzko cvgn{ '' 69' 0Vj gug''f cvc''f go qpuvtcvg''y cv'hkbguv{ ng''ej cpi g''r tqi tco u'o c { ''dg''ko r qtvcpv'hqt''r tko ct { '' r tgxgpvkqp'kp'kpf kxkf wcm'y kj 'f kci pqugf ''ECF ''cpf ''y qug''cv'kpetgcugf ''kum'qh'f kugcug0'Qxgt''y g'' eqwtug''qh''qpg''{gct.''y gki j v'cpf 'DO Kf getgcugf ''¢; '...'f kcuvqnke''dnqqf ''r tguuxtg''f getgcugf ''¢9' ...'' o gcuwtgu''qh''r j {ukecn'hkpguu'kpetgcugf ''47' ...''cpf ''pxgnu''qh'f gr tguukqp''f getgcugf ''pgctn{ ''72' 0'

1b) Global Profiling Status:"""

Gptqmo gpv'vq'vj g'i nqdcn'r tqhkrkpi 'uwwf { 'ku'enqugf "cpf "cm'cevkxg'r ctvkekr cpvu'j cxg'eqo r ngvgf 'vj gkt" r ctvkekr cvkqp'kp'vj g'uwwf {0Gptqmo gpv'kp'vj g'uwd/uwwf { 'y cu'enqugf ''cu''qh'Lwn{ ''49. ''42290F cvc'' cpcn{ uku'ku''qpi qkpi 0''

Uvdlgev'Gptqmo gpv'cpf 'F go qi tcr j keu'"

Uvdlgev'gptqmo gpv'y cu'5960'Vj gtg''y gtg''388'r ctvlekr cpvu'\cmkpi 'r ctv'kp'\y g''khguv{m'ej cpi g'' r tqi tco .''362''uvdlgevu''ugtxlpi ''cu''y g''eqpvtqn'i tqwr .''cpf '8: 'r ctvlekr cpvu''gptqmgf 'kp''y g''Uvd/uvwf {0' F go qi tcr j le''ej ctcevgtkuvleu''qh''y g''eqpvtqn'i tqwr ''y gtg<cxgtci g''ci g''qh'8509''{gctu.''73' ''y gtg'' hgo cng.''4; ' ''y gtg''xgvgtcpu''qt''y g''ur qwug''qh''c''xgvgtcp.''cpf ''56' ''j cf ''f kci pqugf ''EJ F 0''

<u>Fcvc</u><"

"

<u>Nkr qr tqvgkpu</u>''ó''Nkr qUekgpeg''f gxkugf ''y g''pgy ''NR5''cpcn{uku''r tqeguu''q''dgvgt''ceeqwpv'hqt''y g''hwm' f ksgtukv{ ''qh'r ncuo c''hkr qr tqvgkpu''y cv'ur cp''c''eqpvkpwwo ''qh'r ctvkeng''f kco gvgtu''cpf ''c''Nkr qr tqvgkp'' Kpuwrhp'Tgukuvcpeg''Ueqtg''*'NR/KT+:'y j kej 'ku''uki pkhecpvn{ ''cuuqekcvgf ''y kyj ''kpuwrhp''tgukuvcpeg0'Wukpi '' r tgxkqwun{ ''eqmgevgf ''f cvc''kp''y g''Qtpkuj ''cpf ''ETE''r tqi tco u.''y g''hqmqy kpi ''cduvtcev'y cu''r tgr ctgf '' cpf ''uwdo kwgf ''vq''y g''Co gtkecp''Ectf kqmqi {''qh'Ectf kqmqi {<''

Abstract submitted:

Ä Gmuy qtyj 'F N.'O co wrc'MC.'Drcendwtp'J N.'Gpi ngt'TLO.'Xgtpcrku'O P 0'Ectf kce'rkhguv{ng'' kpvgtxgpvkqpu'f khgtkpi 'kp'f kgvct {'uvtkpi gpe{'ko r tqxg'kpuwrkp'tgukuvcpeg'yj tqwi j 'ej cpi gu'kp'' nkr qr tqvgkp'r tqhkrgu0'American College of Cardiology, 64th Annual Scientific Session.'O ctej '' 36/38.'4237.'Ucp'F kgi q.'EC0'

Cduxtcev"

Background: 'O gvcdqrke''f {uhwpevkqp''ej ctcevgtk| gf ''d { ''kpuwrkp''tgukuvcpeg'*KT +'ku''cp''ko r qtvcpv'tkun' hcevqt'hqt''f gxgrqr kpi ''v{r g/4''f kcdgvgu''cpf ''eqtqpct { ''ctvgt { ''f kugcug''*ECF +0'Vj g''Nkr qr tqvgkp'' Kpuwrkp''Tgukuvcpeg''*NR/KT+'ueqtg.''f gtkxgf ''htqo ''o gcuwtgu''qh''rkr qr tqvgkp''uwdercuu''r ctvkerg'' eqpegpvtcvkqp"cpf "ukļ g. "ku"c"pgy "o gcuvtg"hqt"cuuguukpi "KT "cpf "kf gpvkh{kpi "r cvkgpvu"y kj "kpetgcugf" tkumhqt"f gxgqqr kpi "f kcdgvgu0Nkhguv{ng"o qf khecvkqp"kpvgtxgpvkqpu"ctg"npqy p"vq"o gf kcvg"ECF" tkumiyi tqwi j "vtcf kkqpcn"o gcuvtgu"uvej "cu"dnqqf "r tguuvtg."kr kf u."cpf "DO K#j qy gxgt."yj g"ghgevu"qh" f kgvct {"uvtkpi gpe{"qp"KT"cpf "o qngevnct"f tkxgtu"qh"y g"NR/KT"ueqtg"ctg"vpengct0""

Methods: 'Rcvkgpuu'y kj 'ECF ''qt ''uki pkhecpv'ECF ''tkumihcevqtu'r ctvkekr cvgf ''kp''3''qh'4''enkpkecn' nkhguv{ ng'lpvgtxgpvkqpu'f khgtkpi ''kp'f kgvt{ ''uvtkpi gpe{<3+"cp'kpvgpukxg"pqp/tcpf qo k gf ''r tqi tco '' y kj ''c''uvtkev'xgi gvctkcp'f kgv'*p?; 2''uvdlgevu'y kj ''; 2''o cvej gf ''eqpvtqn+"cpf ''4+"c''o qf gtcvg'' tcpf qo k gf ''vtkcn'hqmqy kpi ''c''O gf kgttcpgcp/uv{ ng''f kgv'*p?; 2''r ctvkekr cpvu.''7: ''eqpvtqn+0'Ej cpi gu'' qxgt''3''{ gct'kp''hr qr tqvgkp''r tqhkrgu.''NR/KT''ueqtg.''cpf ''vtcf kkqpcn'ECF ''tkunihcevqtu'y gtg''cuuguugf '' d{ ''Y kreqzqp''Uki pgf 'Tcpni'guvu0''

Results: 'Rctvlekr cpul'kp'yj g'kpvgpukxg'hkguv{ ng'kpvgtxgpvkqp'j cf 'r qqtgt'dcugnkpg''ectf kqxcuewrct'' j gcnj '*uki pkhecpvn{'j ki j gt'DO K'vqcn'ej qnguvgtqn'vtki n{egtkf gu.'NR/KT+'yj cp'r cvkgpvu'kp''yj g'' o qf gtcvg''r tqi tco 0/Dqyj 'kpvgtxgpvkqpu'ngf 'vq''y gki j v'nquu'*/: 0 ' .'kpvgpukxg''r tqi tco =!/408' .'' o qf gtcvg''r tqi tco =!R>2023+"cpf 'c'uki pkhecpv'f getgcug'kp''NR/KT'ueqtg'*/3505' .''kpvgpukxg=!/ 90, ' .''o qf gtcvg=!R>2023+"eqo r ctgf 'vq'tgur gevkxg"eqpvtqnu'qxgt'qpg''{gct0Qh'yj g'ukz'nkr qr tqvgkp'' r ctco gvgtu'yj cv'eqo r tkug'yj g''NR/KT'ueqtg."qpn{'ncti g''XNF Nlej {mo ketqpu'f getgcugf '' uki pkhecpvn{''kp'r cvkgpu'eqo r ctgf 'vq'eqpvtqnu'kp''dqyj 'r tqi tco u'*/4805' .''kpvgpukxg=!/3509' .'' o qf gtcvg=!R>2027+0''

Conclusions: 'Nkhguv{ ng'o qf khecvkqp'kpenvf kpi 'c'O gf kgttcpgcp'f kgv'ku'eqo r ctcdng'vq'c'uvtkpi gpv' kpvgtxgpvkqp'y kj 'c'xgi gvctkcp'f kgv'hqt'ko r tqxkpi 'kpuvrkp'tgukuvcpeg'f ghkpgf 'd{ 'NR/KT0Uki pkhkecpv' tgf wevkqpu'kp'ncti g'XNF Nlej { mo ketqpu'o c{ 'f tkxg'ko r tqxgo gpv'kp''KT'kttgur gevkxg''qh'f kgvct { '' uvtkpi gpe{0''

<u>O cetqr j ci g'o ki tcvkqp'kpj kdkqt { 'hcevqt'*O KH+</u>'6'O KH'ku'cp'kphrco o cvqt { "e{vqnkpg''yj cv'tgi wrcygu" uo qqyj 'o wuerg'egmi'o ki tcvkqp''cpf 'r tqnkhgtcvkqp."cpf ''y wu'r rc{u''cp''ko r qtvcpv'tqrg''kp''r tqo qvkpi " f gxgrqr o gpv'qh''cyj gtquergtqvke''rgukqpu0'O KH'j cu''dggp''uj qy p''vq''dg''cp''ko r qtvcpv''dkqo ctrngt 'hqt" f kugcugu'y kj ''kphrco o cvkqp."uwej ''cu''EXF."f kcdgvgu."qdgukv{."cpf ''ecpegt0'C ''f tchv'o cpwuetkr v'' uwo o ctl{ kpi 'tguwnu''j cu''dggp''r tgr ctgf ''cpf ''cf f kvkqpcn'tgxkukqpu''ctg''qpi qkpi 0'''

<u>I gpg'Gzrtguukqp</u>''ó''Vjg''o cpwætkrv'eqorctkpi ''ej cpigu'kp''igpg''gzrtguukqp''kp''Qtpkuj ''xu'Eqpvtqn'' rctvkekrcpw'ycu''rwdrkujgf ''kp''*Circulation: Cardiovascular Genetics*0'Vjg''tghgtgpeg''ku''rtqxkfgf'' dgrqy <''

Manuscript published (See Appendix A):

•ÁGmuy qtyj 'F N. 'Etqhv'F V'It. 'Y g{cpf v'L 'Uwty| 'NC. 'Drcendwtp'J N. 'Dwtng'C. 'J cdgtmqtp'O L'' O eF {gt'HC. 'Igngo c'I N. 'xcp''Ncct'T. 'O co wrc'MC. 'Xgtpcrku'O P 0'kpvgpukxg''ectf kqxcuewrct'' tkunitgf wevkqp'kpf wegu'uwuvckpcdrg''ej cpi gu'kp''gzr tguukqp''qh'i gpgu''cpf 'r cyj y c{u'ko r qtvcpv'\q'' xcuewrct''hwpevkqp0'Ekte'Ectf kqxcue'I gpgv'4236=9<373/3820''

Cf f kkqpcn'cpcn{ugu''qh'yj g''i gpg''gzr tguukqp''f cvc''j cxg''dggp''eqpf wevgf ''y kyj ''r cvkgpvu''uvtcvkhkgf ''d { " y gki j v''nquu0C''o cpwuetkr v'j cu''dggp''r tgr ctgf ''cpf ''y kn''dg''uvdo kwgf ''vq''yj g''lqwtpcn'*Obesity*''f wtkpi '' yj g''pgzv's wctvgt0Vj g''cduvtcev'cpf ''tghgtgpeg''qh''yj g''r cr gt ''ctg''r tqxkf gf ''dgnqy <''

Manuscript in preparation:

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•ÁGmuy qt y 'F N.'O co wrc'MC.'Drcendwtp'J N.'O eF {gt'HC.'Igngo c'I N.'xcp'Ncct'T.'Gpi ngt'TL'' Xgtpcrku'O P 0'Ko r qtvcpeg''qh'uwduvcpvkcn'y gki j v'nquu'hqt''cnvgtkpi 'i gpg''gzr tguukqp'f wtkpi '' kpvgpukxg"ectf kqxcuewrct"hkhguv{ng"o qf khkecvkqp0'Obesity *vq"dg"uvdo kvgf +0"

Cduxtcev"

Objectives: "Vq"gzco kpg"tgrcvkqpuj kru"dgw ggp'y gki j v'nquu'vj tqwi j "ej cpi gu"kp"nkhguv{ng"cpf " ngwnqe{vg'i gpg"gzr tguukqp"r tqhkrgu0"

Methods: 'C'r tqur gevkxg'pqptcpf qo k gf 'vtcki'y cu'eqpf wevgf ''qxgt''3'' {gct'kp'r ctvkekr cpvu'' wpf gti qkpi ''kpygpukxg''nklguv{ng''o qf khecvkqp''vq'tgxgtug''qt''uxcdkik g'r tqi tguukqp''qh'eqtqpct { "ctvgt { " f kugcug0'Ectf kqxcuewrct'tkum'hcevqtu.''kphrco o cvqt { ''dkqo ctngtu.''cpf ''r gtkr j gtcn'dmqf ''i gpg'' gzr tguukqp''cu'c'hwpevkqp''qh'y gki j v'nquu'y gtg''cuuguugf ''kp'': ; ''hhguv{ng'r ctvkekr cpvu''cpf ''93'' tgvtqur gevkxgn{ ''o cvej gf ''eqpvtqni'wpf gti qkpi ''wuvcn'ectg0''

Results: 'Uwduvcpvkcn'y gki j v'nuu'*/3704_50 ' +'kp'nkhguv{ng'r ctvkekr cpwi*p?55+'y cu'cuuqekcvgf " y kj 'ko r tqxgo gpv'kp'ugngevgf "ectf kqxcuewrct"tkumihcevqtu'cpf 'uki pkhkecpv'ej cpi gu'kp''ngwnqe {vg'' i gpg''gzr tguukqp'htqo 'r tg/'vq''r quv/kpvgtxgpvkqp0Cr r tqzko cvgn{'32' ''qh'y g''tcpuetkr vqo g'*4447'' wpks wg'i gpgu+'uj qy gf ''uki pkhkecpv'gzr tguukqp''ej cpi gu''cv'c'hcnug''f kueqxgt { 'tcvg''eqttgevgf ''P/xcnwg'' >20270Cngtgf ''o qngewrct''r cvj y c {u'y gtg'tgncvgf ''q'ko o wpg''hwpevkqp''cpf ''kphnco o cvqt { 'tgur qpugu'' kpxqrxkpi ''gpf qvj gnkcn'cevkxcvkqp0'Kp''eqpvtcuv.'r ctvkekr cpwi'nqukpi ''o kpko cn'y gki j v'*/508_407' .'' p?54+''uj qy gf ''qpn{''o kpqt''ej cpi gu'kp''ectf kqxcuewrct ''tkumihcevqtu.''o ctmgtu''qh'kphrco o cvkqp.''cpf '' i gpg''gzr tguukqp''eqo r ctgf ''q''pqp/kpvgtxgpvkqp''eqpvtqni''chgt''3''{gct0'''

Conclusions: "Y kf gur tgcf 'i gpg"gzr tguukqp"ej cpi gu"cuuqekcvgf 'y kj "xcuewrct"ko o wpg"cpf " kphrco o cvqt { "tgur qpugu"y gtg"cuuqekcvgf 'y kj "uwduvcpvkcn"dwv"pqv'o kpko cn'y gki j v'nquu"f wtkpi " kpvgpukxg"nkhguv{ ng"o qf khecvkqp"hqt"ectf kqxcuewrct"tkumitgf wevkqp0"

<u>Ut wewtch'cpf "Hwpevkqpch'O gcuwtgu''qh'Ectf kqxcuewrct'J gcnj</u> '6''Ur gekhe 'gpf r qkpu''o gcuwtgf " kpenwf g''glgevkqp''htcevkqp''cpf 'y cm'o qvkqp.''eqtqpct { "ctvgt { "ecrekhecvkqp''ueqtgu.''ngh'cpf 'tki j v' xgpt kewrct'xqnvo gu.'o { qectf kcn'o cuu.'uvgpquku'uk kpi 'cpf 'xguugn'f kco gvgt.''r rcs wg'f gpukv{ "cpf " f khgtgp vkcvkqp''qh'ecrekhgf 'xgtuwu''pqp/ecrekhgf ''r rcs wg.''cpf 'vkuuwg''r gthwukqp''cpf ''xkcdkrkv{0' RGVIE V'uecppkpi ''cpcn{ uku''eqpvkpwgu=eqnrcdqtcvkqp''qpi qkpi ''y kj ''F t0Gf y ctf 'O kngt.''Dquvqp'' Wpkxgtukv{ ''vq''r tqxkf g'enkplecn'lpuki j v'kpvq''f cvc0T guwnu''qh''y g''kpkkcn'cpcn{ uku''kpf kecvg''y cv'o cp{ '' GE V'xctkcdngu''y gtg''uki pkhecpvn{ ''f khgtgpv'dgw ggp''ecugu''cpf ''eqpvtqnu''cv'dcugnkpg.''cpf ''y cv'hgy '' o gcuwtgu''uj qy gf ''uki pkhecpvn{ ''f khgtgpv'ej cpi gu''dgw ggp''i tqwr u0Cpcn{ uku'ku''qpi qkpi 0''

<u>UP R'Xctkcvkqp"cpf 'Qdgukv{</u> '6'F wtkpi 'y g'{gct.'377'uco r ngu'htqo 'kpvgpukxg'hthguv{ng'r ctvkekr cpvu'' y gtg'i gpqv{r gf 'hqt'y g'hqmqy kpi ''qdgukv{/tgrcvgf ''UP Ru<'tu; ; 5; 82; .'tu36432: 7.'tu399: 4535.'' tu4: 37974.'tu96; : 887.'tu364655.'tu; 47; 68.'tu4338: 52.'tu4463645.'tu34666; 9; .'tu876: 45: 0''' ''

<u>F tqr qwu</u>'ó'C''o cpwetkr v'f guetkdkpi 'tgcuqpu'y j { 'r ctvkekr cpw'f kueqpvkpwg'r ctvkekr cvkqp'kp'' nkbguv{ ng''o qf khkecvkqp'r tqi tco u'y cu'eqo r ngvgf 0'Vj g''r cr gt''y cu'tgy tkwgp'htqo ''y g''qtki kpcn'' xgtukqp''vq'hqewu''qpn{ "qp''y g''Qtpkuj ''r tqi tco ''cpf ''vq''gzco kpg'i gpf gt'f khbgtgpegu'kp''cvtkkkqp0'Vj g'' tghgtgpeg''cpf ''cduvtcev'hqt''y g''r cr gt''ctg''r tqxkf gf ''dgnqy 0'Vj g''r cr gt ''y km'dg''uwdo kwgf 'hqt'' r vdnkecvkqp'f wtkpi ''y g''pgzv's wctvgt0''

Manuscript in preparation:

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• ÁO co wrc'MC. "Xgtpcrku'O P. 'Grnuy qtyj 'F NOC wtkskqp'htqo 'htguv{ng'o qfkhecvkqp'r tqi tco u'hqt'' ectfkqxcuewrct'tkum'tgfwevkqp<ti gpfgt''ur gekhe 'eqpukfgtcvkqpu''cpf 'r tgfkevqtu0**q''dg''uwdo kwgf+0''

Cduxtcev"

K gpvkh{kpi 'uki pkhecpv'r tgf levqtu'qh'cwtkkqp'htqo 'hkguv{ng'o qf khecvkqp'r tqi tco u'ku'egpvtcn'q'' ko r tqxkpi 'vtgcvo gpwl'hqt'ectf kqxcuewrt'f kugcug0'Vq'cf f tguu'yj ku'kuwg.'y g''eqpf wevgf ''c'' tgvtqur gevksg''qdugtxcvkqpcn'uwd { ''qh'y qo gp'*p?39: +'cpf ''o gp'*p?382+'y j q''gptqngf 'kp''c''enkpkecn'' nkguv{ng'kpvgtxgpvkqp'f guki pgf ''q''uvcdkrk g''qt'tgxgtug'r tqi tguukqp''qh'j gctv'f kugcug''y tqwi j '' ej cpi gu'kp''tklguv{ng'Rtgrtgcvo gpv'*dcugnkpg+'cpf 'kpkkcn'vtgcvo gpv/tgrcvgf ''xctkcdngu'y gtg'' gzco kpgf 'ugr ctcvgn{''kp'y qo gp''cpf ''o gp''q''cuuguu'wkkv{ ''kp''f kuetko kpcvkpi ''gxgpwcn'f tqr qwu'' htqo ''eqo r ngvgtu0I gpf gt''ur gekhe''uvgr y kug'tgi tguukqp''o qf gm''eqpvckpgf ''y tgg''eqo o qp''xctkcdngu /'q ''eqo r ngvgtu0I gpf gt''ur gekhe''uvgr y kug'tgi tguukqp''o qf gm''eqpvckpgf ''y tgg''eqo o qp''xctkcdngu // dqf { ''o cuu'kpf gz ''cv''gpvt {.''f kgvct { ''eqo r ncpeg.''cpf ''gf wecvkqp''ngxgn''dw''pgkyj gt''o qf gn''ceewtcvgn{'' r tgf kevgf ''cwtkkqp0Ugnhtgr qtvgf 'tgcuqpu'hqt''f tqr r kpi ''qwl'f khgtgf ''dgy ggp'y qo gp''cpf ''o gp<'' pqpeqo r ncpeg'y kji 'yj g''r tqi tco ''i vkf gnkpgu''cpf ''o gf kecnlj gcnj ''r tqdngo u''y gtg''o r qtvcpv'kuwgu'' hqt''y qo gp.''y j kng''y qtnitgrevgf ''eqphnlevu''y gtg''o quv'r tgxcnpv'kp''o gp0Enkplecn'ttkcn''cpf ''hkguv{ng'' r tqi tco u'hqt''ectf kqxcuewret'tkmitgf wevkqp''uj qwf 'tgeqi pk g''y cv'r gtuqpcn'dcttkgtu''q''eqpvkpwgf '' r ctvkekr cvkqp''f khtgt''dgwy ggp''y qo gp''cpf ''o gp''cpf ''o wu'wtxkg''q''ceeqo o qf cvg''cmidcttkgtu'kp'' qtf gt''q''o czko k g''r cvkgpv'tgvgpvkqp0'Vtkcntgi kwtcvkqp'*EnkplecnVtkcn0 qx+<P E V23: 276; 4''''

 $\frac{F \text{ kgvct } (C \text{ pcn} \text{ uku} \text{'b'} \text{'y} \text{ g''qtki kpcn'qdlgevkxg''qh'y ku'r tqlgev'y cu'vq''cuuguu''ej cpi gu'kp'f kgvct } (") eqo r qpgpul'f wtkpi 'y g''ETE''cpf 'Qtpkuj ''r tqi tco u0'Y g'tgegpvt g''gzr cpf g''y g''hqewu''q'kpenvf g'' xkco kp''uwr r go gpu0F wtkpi ''y g''{gct.'f kgvct {''f cvc'y gtg''gpvgtgf ''grgevtqpkecm{ ''cpf ''cpcn{||gf''d{ ''} Hqf ''Rtqeguqt''32082''uqhy ctg''r tqi tco ''hqt'': 7'' ctvkek cpu''cv'5''vko g''r qkpwu''gcej '*477'' s wguvkqppcktgu+0Hqf ''Rtqeguqt''tguwnu''y gtg''gpvgtgf ''kpvq''y g'Ceeguu'f cvcdcug0Cpcn{uku''qh'' f kgvct{''ej cpi gu''uj qy gf ''y g''hqmy kpi <*3+'uki pkhecpv'ej cpi gu''kp''qvcn'ecmtkgu'*/35' +.'' ''ecmtkgu'' tqo ''hcv'*/78' +.''cpf'' ''ecmtkgu''htqo ''ectdqj {f tcvgu'*_4: ' +'f wtkpi ''kpvgpukxg''hkguv{ rg'ej cpi g='' *4+''uki pkhecpv'ej cpi gu''kp''y g''hqmy kpi ''f kgvct{''eqo r qpgpux</texter thqo ''ucwtcvgf 'hcv'*/97' +.'' f kgct{''hdgt'*_83' +.''o qpq/wpucwtcvgf ''hcv'*/92' +.'' qn{/ucwtcvgf 'hcv'*/5; ' +.''tcpu''hcwl*/98' +.'' ej qrguvgtqn'*: 9' +='*5+''uki pkhecpv'ej cpi gu''kp''xkco kpu<C''*_5; ' +.''D8'*_4; '' +'E'*_5: ' +.''M'' *_ ; 9' +0C''ny 'hcv'f kgv'r tqxkf gu''o qtg''o kpgtcm''y cp''c''j ki j /hcv'f kgv0Eqo r ctkuqpu'y kj ''y g''ETE'' rtqi tco ''c'g''p'' tqu tguu0''$

 $\begin{array}{l} Cp"cpcn{uku'qh'f kgvct{"tceg"gngo gpu'uj qy gf <ktqp"*_63' "ej cpi g."R? 2023+"| kpe"*_7' "ej cpi g." R? 20533+"eqr r gt"*_52' "ej cpi g."R? 202: 9+."o cpi cpgug"*_; ; ' "ej cpi g." R> 2023+."ej tqo kwo "*_36' "ej cpi g." R? 209; 8+."o qn{df gpwo "*_37' "ej cpi g." R? 209: +'f wtkpi "httpuv{ng"o qf ktkec.tqp0" F cvc"gpvt{"htt"xkco kp"kpvcng"cv'dcugrkpg."34"y ggmu."cpf "3"{gct"ku'qpi qkpi 0""$

2) Cardiovascular Risk Assessment and Prevention Program through the Cardiovascular Risk Clinic (CRC)

<u>O gyj qf qmji {</u><"

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Vj ku'r tqi tco ''y cu'guvcdrkuj gf ''cu''c'r nevhqto ''vq''cf f tguu''y g''wpks wg''pggf u''qh'tgvktgf ''o krket { '' dgpghleketrkgu''cv'tkumlhqt''EX''f kugcug0'Vj g''r tqi tco ''o kttqtu''y g''Ectf kce''Rtgxgpvkqp''Rtqi tco ''*ERR+'' f guki pgf ''cpf ''guvcdrkuj gf ''d{ ''y g''KEJ R''cv'Y TCO E0'Ki'kpenwf gu''eqpxgpvkqpcn''cpf ''pqxgn'EX'tkum'' r tqhkrkpi ''cpf ''ckrqtgf .''r gtuqperrk gf ''dgj exkqteritgeqo o gpf evkqpu'hqt''r tko et { ''qt''ugeqpf et { '' r tgxgpvkqp''d{ ''cp''kpvgi tevkxg''vgco ''qh''r tqxkf gtu''eqo r tkugf ''qh''c''pwtug''ecug''o cpci gt. ''r u{ej qrqi kuv.'' pwtug''r teevkxkqpgtu. ''f kgvkkepu.''uvtguu'o cpci go gpv'kpuvtwevqtu.''cpf ''gzgtekug''r j { ukqrqi kuv0' Xerkf evgf ''qqnu''q''uetggp''hqt''cpf ''o gcuwtg''EX''tkum''uvtguu.''urggr ''j genj .''eqo r rkepg'y kj ''f kgvet { '' tgeqo o gpf evkqpu''epf ''gzgtekug''etg''uvcpf etf ''qh''ectg0'Vj g''r tqi tco ''ku''ep''ef lwpev'vq''y g''dguv'' o gf keen'r teevkegu''r tqxkf gf ''d{ ''y gkt''r tko et { ''ectg''r tqxkf gt0''''' Rj cug'Kqh'y g''r tqi tco 'kpxqnxgu''gcej ''r ctvkekr cpv'wpf gti qkpi ''c''eqo r tgj gpukxg''j gcnyj ''tkum' cuuguuo gpv'y cv'ku''eqo r ngvgf ''d { ''c''r j {ukekcp. ''hqmqy gf ''d { ''c''hqwt/''j qwt''õRgctnu''hqt''{ qwt''J gctvö'' y qtmij qr ''cpf ''r ctvkekr cpwu''y gp''uej gf wrg''kpf kxkf wcn'cr r qkpvo gpwu'y kj ''gcej ''o qf crkv{ ''ur gekcrkuv'' vq 'tgegkxg''gf wecvkqp''cpf ''eqwpugrkpi ''kp''pwtkkqp. ''gzgtekug. ''utguu''o cpci go gpv''cpf ''o kpf kdqf { j gcnyj 0'Vj gug''ctg''o qpyj n{ ''cr r qkpvo gpwu''q''dg''eqo r ngvgf ''qxgt''c''6/8''o qpyj ''r gtkqf 0''''

Rj cug''KKqh' y g''r tqi tco "dgi kpu''chygt ''y g''eqo r ngvkqp''qh' y g''j gcnj { ''hhguv{ ng''kpvgtxgpvkqp'*Rj cug''K0'' F wtkpi ''y ku''r j cug''gcej ''r ctvkekr cpv' y km''ci ckp''o ggv' y kj ''y g''r j { ukekcp0F wtkpi ''y ku''cr r qkpvo gpv'' y g''r j { ukekcp''y km''r tgr ctg' y g''r ctvkekr cpwu''hqt''y g''pgz v'r j cug''cpf ''i kxg''y go ''uvtcvgi kgu''hqt'' o ckpvckpkpi ''uweeguu''qp''y gkt''qy p0'Vj g''ugeqpf ''r j cug''qh' y g''Rtqi tco ''r tqxkf gu''cf f kkqpcn'' tgkphqtego gpv' y tqwi j ''o qpy n{ ''r j qpg''ecmu'y ky ''cp''kpvgi tcvkxg''j gcnj ''eqcej 0'Rctvkekr cpwu'y km'' tgo ckp''kp''Rj cug''4''hqt''hxg''{ gctu. ''f wtkpi ''y j kej ''vko g''y g{ ''y km''eqo g''q''y g''egpvgt''hqt''tg/ cuuguuo gpwu''gxgt { ''ukz''o qpy u0

<u>Status</u><""

"

Gptqmo gpv'kp''y ku'r tqi tco ''gpf gf 'Lwpg''52.''4235='f cvc''cpcn{uku'ku''qpi qkpi 0''' Uvdlgev'Gptqmo gpv'cpf 'F go qi tcr j keu<''

F go qi tcr j ke"ej ctcevgtkuvkeu"qh"r ctvkekr cpwi'y gtg<"cxgtci g"ci g"7: 0, "{gctu."7: ' 'hgo crg."44' " xgvgtcpu"qt'y g'ur qwug"qh'c'xgvgtcp."cpf "42' ''y kj "f kci pqugf "eqtqpct {'j gctv'f kugcug0'Vqvcn' uwdlgev'gptqmo gpv'y cu"486"*366'kpvgtxgpvkqp=342"eqpvtqnu=7; "f tqr/qwu=56"eqpvtqn" r ctvkekr cpwi'vtcpuhgttgf ''q"y g'kpvgtxgpvkqp"cto "chvgt"qpg"{gct"cu"c'eqpvtqn0'C'uwo o ct {''qh'hkpcn'' r cvkgpv'r tqi tguu'ku'cu'hqmqy u<"

/''346''kpvgtxgpvkqp''r ctvkekr cpvu''eqo r ngvgf ''y g''kpvgtxgpvkqp''*6/8''o qpy u="324"eqo r ngvgf ''htuv'8'' o qpy i'hqmqy /wr ''ko g''r qkpv="8: "eqo r ngvgf ''{gct''3="67"tgcej gf ''o qpy ''3: ="48"tgcej gf ''{gct''4="36" eqo r ngvgf ''O qpy i''52="33"j cxg"eqo r ngvgf ''{gct''50"'

/"; 3"eqpvtqnı"eqo r ngvgf "ý g"õy ckkpi "r gtkqf "eqo r ngvgö" ko g"r qkpv *8"o qpy u = 88"eqo r ngvgf "ý g" hktuv '8^ý "o qpy 'hqmqy /wr 'ko g"r qkpv = 4; "tgcej gf "{gct '3 = 43"eqo r ngvgf "o qpy '3: = 33"tgcej gf "{gct "4 = : 'j cxg"eqo r ngvgf "{gct '50"

/"; 2"kpvgtxgpvkqp"r ctvkekr cpv'ucvkuhcevkqp'uvvtxg{u'y gtg"eqo r mygf "cpf "tgvvtpgf"

C''dcvej ''qh'37''uco r ngu''hqt''r ncuo c''o ctngtu''ngr vkp. ''kpuwrkp. 'j uETR. ''cpf ''i nxequg=''35''uco r ngu''hqt'' ugtwo ''o ctngtu''cf kr qpgevkp. ''ugtwo ''co { ngkf ''C. ''xkco kp'F. ''cpf ''r *c+''kpenwf kpi ''c''wpkxgtucn'eqpvtqn'' uco r ng''y gtg''ugpv''vq''Nkr qUekgpeg''cpf ''Lqj pu'J qr nkpu0''

<u>I gpg'Gzrtguukqp</u>''6''Vjg'TPC'htqo''7; 'ETE''dnqqf''ucorngu'ycu'kuqncvgf''htqo''RCZigpg''wdgu.'' i nqdlp''engctgf.''cornkhgf.''htci ogpvgf.''cpf''ucoppgf''qp''W355C''4@''gzrtguukqp''cttc{u0Ecm'tcvgu'' ygtg'7205/8406' 0'Cp''cffkkqpcn'54''ETE''ucorngu'jcxg''dggp'kuqncvgf''cpf''i nqdkp''engctgf0TPC'' eqpegpvtcvkqpu'tcpigf''htqo''540/3;:07''pilµn='QF48214:2'tcvkqu'ygtg''402:/404;='TKP''pwodgtu'' ygtg'90/;040''

F O GV"cttc {u'y gtg"twp"qp"F P C "uco r ngu"htqo "62"ETE"r ctvkekr cpvu="ecmttcvgu"y gtg"; : 046/ ; ; 0,2' 0'Vj ktv{/qpg"ETE"uco r ngu"y gtg"i gpqv{r gf "wukpi "w q"Vcs O cp"UP R"cuuc {u<tu34666; 4; " cpf "tu36432: 70"

 $\underline{UP R'xctkcvkqp''cpf''tki n{egtkf gu''6'I gpqv{r kpi ''qh'339''ETE''r ctvkekr cpvu''eqo r gvgf''hqt''3; ''UP Ru'' r qvgpvkcm{''cuuqekcvgf''y kj ''vtki n{egtkf g'tgur qpug0'Ucvkuvkecnl'cpcn{uku''ku''qpi qkpi 0'''''$

Task #6: Initiate "Exploring the Predictive Patterns of the Natural History of Pre-diabetes: Proof of Principle Study" protocol at WRNMMC (PI – COL Robert Vigersky, Diabetes Institute).

<u>O gyj qf qmji {</u>"

Vj g''r tlo ct { ''r wtr qug''qh'y ku'r tqur gevkxg. "qdugtxcvkqpcn'r tqqh'qh'r tlpekr g''uwf { 'ku'vq'f gvgto lpg'y g'' hgculdlktk{ ''qh'wulpi ''c''pqxgn'r qlpv/qh/ectg'%lQ0j qo g+."o wnkr m"cpcn{vg'vguv'r mvhqto ''%Vj gtcpqu+'vq'' uwf { ''y g'vgo r qtcn'ej cpi gu'lp 'hkxg''dlqo ctmgtu'tgmvgf 'vq''i nwequg'f { utgi wmvlqp. 'lphnco o cvlqp.'' xcuewmt 'f { uhwpevlqp. ''cpf 'ko o wplx{ ''y cv'ecp''ngcf ''vq'f kcdgvgu''cpf 'lpetgcugf ''ectf lqxcuewmt'tlum']kpuwrkp. ''ngr vkp. 'j ki j ''ugpukkkxk{ ''Vtqr qplxp''V'*j u/eVpV+.'j ki j ''ugpukkxkx{ ''E/tgcevkxg''r tqvgkp'*j u/ETR+." cpf 'hgttkkp_0C''ugeqpf ct { ''r wtr qug'ku''q''gzco kpg''r cwgtpu''qh'i gpg''gzr tguulqp''kp''r gtkr j gtcn'dmqf ''kp'' r cvlgpvu''f kci pqugf ''y kj ''r tg/f kcdgvgu'y j q''ctg''gpvgtkpi ''kpvq''cp''kpvgpukxg''rkbguv{ m''o qf khecvlqp'' r tqi tco 0''

Wr '\q'72''cf wn/'o ktkct { 'j gcnj ectg''dgpghlekctlgu'*@3: "{gctu+'y j q'o gv'y g''uetggpkpi ''etkgtkc'hqt''r tg/ f kcdgvgu''cpf 'j cxg''ugn/tghgttgf ''qt''dggp''tghgttgf ''q''y g''REJ R/ERR'hqt''EX''tkunitgf wevkqp''y kni'dg'' gptqmgf 0Gcej ''r ctvlekr cpv'y kni'dg''r tqxkf gf ''c''r qtvcdng. 'j qo g/dcugf ''Vj gtcpqu'u{uvgo ''cpf ''dg''cungf ''q'' r tqxkf g'c'hlpi gtuvlemi*HU+'dmqf ''uco r ng''q''y g''u{uvgo ''cv'y tgg''ur gelthe ''vlo gu''r gt ''y ggnihqt''4''o qpy u'' r tg/kpkkcvkqp''cpf ''hqt''y g''f wtcvkqp''qh'y gkt''r ctvlekr cvkqp''kp''y g''htguv{ng''ej cpi g''r tqi tco 0'' Dmqf ''uco r ngu'y kni'dg''eqmgevgf ''r tkqt''q'*4''o qpy u+''cpf ''cv'y g''eqpenvukqp''qh''y g''htguv{ng''r tqi tco '' * ''o qpy u+''q'gxcnwcyg''ej cpi gu'kp'' gpg''gzr tguukqp''cpf ''q''f gvgto kpg''ej cpi gu'kp'y g''dkqo ctmgtu'' pqvgf ''cdqxg0'Dmqf ''uco r ngu'y kni'dg''eqmgevgf ''ci ckp''cv'34. ''46. ''cpf ''58''o qpy u''q''f gvgto kpg''kh'' y gtg''ctg''cf f kkqpcn'ej cpi gu'kp''y g''i gpgvke''o ctmgtu''cpf ''kh'y g''dkqo ctmgtu''ctg''c''o gcuvtg''qh'y gkt'' f {ui n{ego kc0'''

C'xctkgv{ "qh'uvcvkuvkecn'vgej pks vgu'y km'dg'vugf.'f gr gpf kpi "qp'y g'ngxgn'qh'o gcuwtgo gpv'qh'y g" xctkcdngu'y g'ctg'o qf gnkpi '*g0 0'dkpqo kcn'o wnkpqo kcn'eqpvkpwqwu+'vq'ej ctcevgtk g'y g'f {pco ke'' tgncvkqpuj kr 'dgwy ggp'vj g'cpcn{vgu'qdvckpgf ''d{ ''y g''Vj gtcpqu'u{uvgo ''cpf ''3+''o gvcdqnke''cpf ''EX'tkun'' cpf ''4+''cf xcpego gpv'vq'f kcdgvgu''cpf lqt ''EXF 0''''

Status:""

Y TPO O E'r tqvqeqnluwdo kwgf ''q'F TR''qp''; 'O c { ''34''cpf ''KTD''cr r tqxcnltgegkxgf ''qp''8'F ge''34'' y kj ''uwdugs wgpv'4^{pf} ''ngxgnl'cr r tqxcnld { ''WUCO TO E ''J TRQ''qp''6'Lwp''350'Vj g''Y TKr tqvqeqnly cu'' cr r tqxgf ''d { ''y g''Y O E ''KTD''qp''39''O c { ''35''cpf ''d { ''y g''WUCO TO E ''J TRQ''qp''46''Lwn{ ''42350'Vj g'' Y TKr tqvqeqnly cu''y gp''uwdo kwgf ''q''y g''Ej gucr gcng''KTD''qp''O ctej ''32.''4236.''y j q''f gvgto kpgf '' y cv''y ku''uwf { ''y cu''pqp/j wo cp''uwdlgev'tgugctej ''cv''Y TK0'Uwd''cy ctf ''hqt I gpgxc''Hqwpf cvkqp'' gz gewgf ''cpf ''uwf { ''r ncppkpi ''j cu''dgi wp=''cy ckkpi ''gz gewkqp''qh''Vj gtcpqu.''Kpe0'eqpvtcev0'Rncp'' co gpf o gpv'uwdo kuukqp''q'encth{ ''yo r qtct { ''dnqf ''uvqtci g''ngcvkqp''cv''Y TP O O E ''cpf ''wr f cvgf '' KEJ R''htguv{ ng''r tqi tco ''uwtxg{ ''qnn0Tgetwko gpv'ku''r gpf kpi 0'

<u>Task #7: Continue study entitled "Metabolic and Biomolecular Biology Study Studies in</u> <u>Surgical Interventions for Morbid Obesity</u>" as a component of the Integrative Cardiac Health Program at WRI.

<u>O gyi qf qnqi {</u>"

"

Vj ku'uwf {'tgr tgugpw'c'eqncdqtcvkqp'kpxqnxkpi 'Y TK'Y kpf dgt''Uwti gt {'Egpvgt.''cpf 'Y TPOOE0' Vj g'r wtr qug''qh'yj g''uwf {''ku'vq''ej ctcevgtkj g'*3+''dkqo qngewnct''r tqhkngu'kp''cf kr qug''vkuuwg''cv'dcugnkpg'' yj cv'ctg''r tgf kevkxg''qh''uki pkhkecpv'f khngtgpegu''co qpi ''kpf kxkf wcnu'kp''tcvgu''qh''hwwtg''y gki j v''quu.''cpf '' *4+'nqpi kwf kpcn'dkqo qngewnct''ej cpi gu'kp'r gtkrj gtcn'dmqqf ''y cv'eqttgncvg''y kj 'tcvgu''qh'y gki j v'nquu'' kp''qdgug'r cvkgpvu0''

<u>Status:</u>

"

F wtkpi ''y g''{gct.''pq''pgy ''rcr/dcpf ''r cvkgpwi'y gtg''eqpugpvgf ''q''r ctvkekr cvg''kp''y g'tgugctej ''uwf {0' Hqmqy /wr ''dmqf ''uco r ngu'y gtg''qdvckpgf ''htqo ''69''r ctvkekr cpwi'cpf ''886''r ncuo c ITDE ''cnks wqwi'y gtg'' r tqeguugf ''cpf ''uqtgf =''334''r ncuo c''cnks wqwi'hqt ''gcej ''dkqo ctngt.''y j kej ''kpenwf gf ''c''wpkxgtucn'' eqpvtqn''y gtg''ugpv'vq''Nkr qUekgpeg'hqt ''rkr qr tqvgkp''cpcn{uku''cpf ''Iqj pu''J qr nkpu''Dc { xkgy ''O gf kecn'' Egpvgt ''hqt''ngr vkp. ''kpuwrkp.''j uETR.''cpf ''i nwequg''yguvkpi 0'''

Drqqf 'TPC''uco r ngu'htqo ''432'r cvkgpvu'y gtg''i nqdkp/engctgf.''co r nkhkgf.''cpf ''twp''qp''i gpg'' gzr tguukqp''cttc{u0'Ecm'tcvgu''qp''gzr tguukqp''cttc{u''y gtg''7309/8407' 0TPC''eqpegpvtcvkqpu''y gtg'' 4303/43: 07''pi 1µn''QF48214: 2'tcvkqu''y gtg''4028/4048='TKPu''y gtg''902/; 080'Y g''ctg''y ckskpi ''hqt'' o ketqcttc{u'vq''eqo r ngvg''y g''gzr tguukqp''cpcn{uku0''

F wtkpi ''y g''{gct.'95''uco r mu'htqo ''NCI D'r cvkgpvu''y gtg''i gpqv{r gf 'hqt''y g'hqmqy kpi ''qdgukv{/ tgrcvgf ''UP Ru<'tu; ; 5; 82; .'tu36432: 7.'tu399: 4535.'tu4: 37974.'tu96; : 887.'tu364655.'tu; 47; 68.'' tu4338: 52.'tu4463645.'tu34666; 9; .'tu876: 45: 0F P C ''y cu'kuqrcvgf 'htqo ''67''dmqf ''uco r mu='' eqpegpvtcvkqpu''y gtg'909/54608''pi lwn''QF 48214: 2'tcvkqu''y gtg''30 ; /40490'''

Vj g'r gtegpyci g''qh'gzeguu''dqf { 'y gki j v'nquu'* GDY N+'y cu''ecnewncygf 0'Vtgpf u'kp''nqpi /vgto " y gki j v'nquu'y gtg''gzco kpgf 'd{ 'tcpf qo ''eqghhkelgpyu''o qf gni'cpf ''Mtwnncn'Y cmku'Tcpm/Uwo ''Vguvu0' Tguwnu''uj qy ''y cv'y gtg''ku''pq''uki pkhecpy'gxlf gpeg'*, 7' ''eqphkf gpeg''ngxgn+'y cv'y gtg''ctg'' f khgtgpegu''p'' GDY N'cetquu''vko g''r qkpyu'hqt''y g''i tqwr ''cu''c''y j qng.''qy gt''y cp''y cv'y g''qxgtcm'' i tqwr ''gzr gtkgpegu''r qukxkxg'' GDY N'y kj 'tgur gev''q''dcugrkpg0'Chygt'8''o qpy u ''uki pkhecpy'' ej cpi gu'kp'' GDY N'f kf ''pqv'qeewt0'





<u>Eqorctkuqp''qh'hkrqrtqvgkp''ejcpigu''kp''c''uwtikecn'kpvgtxgpvkqp''xu''hktguv{m''oqfkhecvkqp</u>''ó''Vjg'' hqmqy kpi ''cduvtcev.''y jkej ''eqorctgf''hkrqrtqvgkp''ejcpigu''hqmqy kpi ''c''uwtikecn'kpvgtxgpvkqp''xu'' nktguv{m''oqfkhecvkqp.''y cu''rtgugpvgf''cu''c''rquvgt''cv''yg''Qdgukv{''Uqekgv{''oggvkpi<'''

Abstract presented as poster:

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/" Drcendwtp'J N.'O co wrc'MC.'J cdgtmqtp'O L'Dwtng'C.''UrcxknilG.''Ucpp'P L'O ctng{"MT.'' Xgtpcrku'O P.'Grny qty 'F N0F khgtgp\kcn'ghge\xgpguu'qh'rcr ctqueqr kecm{/cf lwucdng'i cuvtke'' dcpf kpi 'xgtuwu'rkhguv{ng'o qf khecvkqp'hqt'o qf kh{kpi 'r rcuo c'rkr qr tqvgkp'r tqhkrgu0'Obesity 2013: 31st Annual Scientific Meeting.'P qxgo dgt''33/38.''4235.'Cvrcpvc.'I C0''

Cduxtcev"

Qdgukv{ 'ku'cp'ko r qt vcpv'ectf kqxcuewrct'f kugcug'*EXF +'tkum'rcevqt'ko r nkecvgf 'kp'f {unkr kf go kc'cpf " xcuewrct''f {uhvpevkqp0Cnj qwi j 'NF N'nqy gtkpi 'ku'qhvgp'c'r tko ct {'i qcn'qh'y gtcr {.'y g'uk g'cpf " eqpegpvtcvkqp''qh'nkr qr tqvgkpu'r tqxkf g''cf f kkqpcn'kphqto cvkqp''qp''y g'vtwg''cy gtqi gpkekv{ "qh'r rcuo c" nkr kf u0Uvti kecn'cpf 'hkhguv{ ng'kpvgtxgpvkqpu''ctg''qr vkqpu'hqt'y gki j v'nquu.''dw'nkvvg''ku''npqy p''cdqw' y gkt''ghhgewi'qp''hr qr tqvgkpu0'''''''

Ej cpi gu'kp'DO Kcpf 'r nœuo c'hr qr tqvgkpu'qxgt '3''{gct 'y gtg''eqo r ctgf 'dgw ggp'53'r cvkgpvu'' wpf gti qkpi 'nœr ctqueqr kecm{ 'r nœgf 'cf lwuxcdng'i cuxtke''dcpf kpi '*NCI D+'cpf ''o cvej gf 'r ctvkekr cpvu'' kp'4''hkguv{ng''ej cpi g''r tqi tco u'f khgtkpi 'kp'ueqr g'cpf 'kpvgpukv{0Nkr qr tqvgkp''r tqhkngu'y gtg'' f gvgto kpgf ''d{ ''pwengct ''o ci pgvke''tguqpcpeg'*P O T+'ur gevtqueqr {0Dcugnkpg''xcnvgu'y gtg''eqo r ctgf '' wukpi ''Y kneqzqp''Uki pgf 'Tcpni'vguvu'hqt''o cvej gf ''r cktu=''ej cpi gu''qxgt''ko g'y gtg''cuuguugf ''d{ ''r cktgf '' v vguv0'''

 $\begin{array}{l} Qxgt"3"{gct."NCI D"rgf" \q"uki pkhlecpvn{"rqy gt"DO K*/38' ."r > 2023"xu"dcugnlpg+"vj cp"kpvgpulxg"*/ : '."r > 2023+"qt"o qf gtcvg"*/4' ."r > 2027+"hlguv{rg"ej cpi g"*o cvej gf/r cktu"r > 2023"kp"dqvj " eqo r ctkuqpu+0P qvcdn{."rkr qr tqvgkp"tgur qpugu"f khlgtgf "dgwy ggp"kpvgtxgpvkqpu0Tkpvgpulxg"hlguv{rg" rgf "vq"enkplecn"ej cpi gu"kp"vqvcn"NF N"r ctvkergu"*632' ."r > 2027"xu"dcugnlpg"cpf "o cvej gf "r cktu+." y j krg"NCI D"tguvngf "kp"c"uki pkhlecpv"kpetgcug"kp"J F N"r ctvkergu"*- 3; '."r > 2023+"xgtuvu" kpvgpulxg"*68' ."r > 2027+"hllguv{rg" rgf "vq"enkplecn"ej cpi g"*o cvej gf "r cktu+."$

NCI D'uwti gt { "cpf "hthguv{ ng"ej cpi g"ngf "vq'y gki j v"nquu"cpf "ej cpi gu"kp"hkr qr tqvgkp"uwdencuugu=" j qy gxgt. "yj g"kpvgtxgpvkqpu"o c { "chhgev"EXF "tkum"yj tqwi j "fkhgtgpv"r cyj y c { u0"Nkhguv{ ng"tgf wegf " yj g"cyj gtqi gpkekv{ "qh"NF N"hkr qr tqvgkpu. "y j kej "o c { "kpj kdkv"kphrco o cvkqp"cpf "gpf qyj gnkcn" f {uhwpevkqp0'I cuvtke''uwti gt {'ko rtqxgf ''y g''pwo dgt''qh''J F N''r ctvkengu''cpf ''o c { ''r tqvgev'ci ckpuv'' EXF ''y tqwi j ''cpvk/kphrco o cvqt { ''cpf ''cpvkqzkf cpv''cevkxkkgu0'''

Task #8: Initiate the "Global Profiling of Gene/Protein Expression and Single Nucleotide Polymorphisms Associated with Coronary Heart Disease Reversal: Long-term Follow-up Sub-study at WRI.

<u>Ogyiqfqmqi {</u>"

Uwf {"ku"cuuguukpi "nqpi /vgto "o ckpvgpcpeg"*5/9- "{gctu+"qh"ugngevgf "r j {ukecn'r ctco gvgtu." r u{ej qo gvtke"o gcuwtgu."r ncuo c"hr kf u."cpf "r gtkr j gtcn'dnqqf "i gpg"gzr tguukqp"kp"r cuv'r ctvkekr cpvu" qh'yj g"Qtpkuj "Rtqi tco "vq"vpf gtuvcpf kpi "y j gvj gt"vtcf kkqpcn'tkum'hcevqt"cpf "o qngewrct"ej cpi gu" r gtukuv'qxgt"vko g"cpf "eqpvtkdwg"vq"nqpi /vgto "tkum'tgf wevkqp0"

Status:

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Vj tgg"gzco kpcvkqpu'y gtg"eqpf wevgf 'hqt"r cuv'r ctvkekr cpvu="gzco u"eqpukuvgf "qh'dmqqf "f tcy ." r u{ej qo gvtke"uwtxg{u."uvcpf ctf "cpvj tqr qo gvtke"o gcuwtgo gpvu."cpf "5/f c{"f kgvct {"tgecm0" Tgetvkko gpv'ku"eqo r mgvg="c"vqvcn"qh'6; "r ctvkekr cpvu"gptqmgf "kp"vj g"uvvf {0"

Hqt"cml6; 'r ctvkekr cpvu."eqngevgf "cpf "eqnrcvgf "cmlf cvc"hqto u."eqo r ngvgf "cmlhqqf 'f kctkgu'kp"Hqqf " Rtqeguuqt."ueqtgf 'r u{ej quqekcn'uvtxg{u."cpf "gpvgtgf "cmlf cvc"kpenvf kpi "o gf kecvkqp kkco kpu"cpf " r j {ukecn'cuuguuo gpv'hqto u'kpvq"yj g'f cvcdcug06; "TPC"uco r ngu'htqo "nqpi /vgto "uvvf { 'r ctvkekr cpvu" y gtg"kuqncvgf."i nqdkp"engctgf."co r nkhgf."cpf "htci o gpvgf ="eqpegpvtcvkqpu"y gtg"3: 0,/3470 "pi lµn" QF 48214: 2'tcvkqu'y gtg'4023/4049="TKP u'y gtg'90/; 020CmlTPC"uco r ngu'y gtg'twp"qp"W355C"402" gzr tguukqp"cttc{u'y kj "ecml'tcvgu"@7: 073' 0Cpcn{uku"qh'i gpg"gzr tguukqp"y kmldg"eqpf wevgf "f wtkpi " y g"pgzv's wctvgt0"

References:

- 30ÁUj cj tkct "U.'O cuwo k'O.'Gf lvgj cf k'H "gv'cn0'Ectf kqxcuewnct "tkunihcevqtu"co qpi "o cngu"y kj "y ct/ tgncvgf "dkncvgtcn'nqy gt"nko d"co r wcvkqp0'*Mil Med.* 422; =396*32+332: /330'
- 40Â O qf cp'O ."Rgrgu'G."J cmhp'J ."gv'cn'hpetgcugf "ectf kqxcuewrct"f kugcug"o qtvcrkv{ 'tcvgu'kp" vtcwo cvke"nqy gt 'ho d"co r wggu0'Am J Cardiol03; ; : = 4*32+3464/90"
- 50Á Mqpgu'T0O qrgewrct'uqwtegu'qh'tgukf wcn'ectf kqxcuewrct'tkum'enkpkecn'uki pcnu."cpf 'kppqxcvkxg" uqnwkqpu<'tgrcvkqpuj kr 'y ky 'uwdenkpkecn'f kugcug.'wpf gt vtgcvo gpv."cpf 'r qqt"cf j gtgpeg<" ko r nkecvkqpu'qh'pgy "gxkf gpeg'wr qp"qr vko k kpi "ectf kqxcuewrct'r cvkgpv'qweqo gu0Vasc Health Risk Manag04235≒ <839/920Gr wd''4235'Qev'430Tgxkgy 0'Qpnkpg"cv" j wr ⊲ly y y @pedk@pm @pkj @ qx lr o e lctvkenguIRO E5: 2: 372"
- 60Á Mcuj cpk'O. 'Grkeuuqp'C. 'Xgtpcrku'O. 'Equxe'N. 'Vgtj cct'O 0'Kor tqxkpi ''cuuguuo gpv'qh'' ectf kqxcuewret'f kugcug'tkum'd { ''wukpi 'hco kn{ ''j kuvqt { <cp'kpvgi tcvkxg''rkgtcwtg''tgxkgy 0'J Cardiovasc Nurs0'4235'P qx/F ge=4: *8+G3: /490'f qk<32082; 9 ILEP 02d235g53: 4; 6d4280'
- 70ÁI qhh'F E'Lt.'Nıq {f/Lqpgu'F O.'Dgppgw'I.'gv'cn04235'CEE ICJ C'i wkf gnkpg''qp''y g''cuuguuo gpv'' qh'ectf kqxcuewrct''tkum*c'tgr qtv'qh'y g'Co gtkecp'Eqnrgi g''qh'Ectf kqnqi {1Co gtkecp'J gctv'' Cuuqekcvkqp''Vcum'Hqteg''qp''Rtcevkeg'I wkf gnkpgu0'*Circ*.''4236'Lwp''46=34; *47''Uwr r n'4+U6; /950' Gr wd''4235'P qx''340'
- 80ÁNVI 'Rcvtkekc'J qtqj q'*WU'Cto { 'Uvti gqp'I gpgtcn+0'Vguvko qp{ 'qp'F ghgpug'J gcnj 'Rtqi tco " dghqtg'\j g'Uvdeqo o kvgg'qp'F ghgpug'qh'\j g'J qwug'Eqo o kvgg'qp'Crrtqrtkcvkqpu.'J qwug'qh' Tgrtgugpvcvkxgu.'335^{\j} 'Eqpi tguu.'Crtktl4.''4236'*Tgeqtf gf 'Xgtukqp+0Tgvtkgxgf 'htqo " <u>j wr ⊲lcto {o gf kekpg0 knlF qewo gpvulNVI /Rcvtkekc/J qtqj q/Y tkvgp/Vguvko qp{0 f h</u>0'Ceeguugf " 49'Cwi wuv'42360'

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Key Research Accomplishments

DC VVNG"Vtkcn"

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- •Á Rquvgt 'r tgugpvgf ''cv'vj g'CJ C 'GRKIP RCO ''4236''Uekgpvkhke''Uguukqp''cpf ''r wdrkuj gf ''kp'' Circulation<''
 - A Y chł gt 'GO . 'Xgtpcrku'O P . 'O qf nkp 'TG0'kphwgpeg''qh'EKO V'cu'c'o qvkxcvqt 'hqt'j gcnj " dgj cxkqt''ej cpi g'kp''c'j gctv'j gcnj 'r tqi tco 0'*Circ*. 4236=34; <CR3480*.''Ucp''Htcpekueq." EC. 'O ctej '3; . ''4236+''

Eqortgj gpukxg'Ectfkqxcuewrct'Tkum'Cuuguuo gpv'cpf'Rtgxgpvkqp'Rtqitco '*EJ R+''

- Á Rcr gt 'r wdrkuj gf 'kp'Sleep Breath''
 - A Grkcuuqp'C. 'Mcuj cpk'O. 'O qf rkp'T. 'J qy ctf 'T. 'Xgtpcrku'O 0Hcvki wgf 'qp'Xgpwu." Urggr { ''qp'O ctuô I gpf gt ''cpf ''tcekcn'f khgtgpegu'kp''u{o r vqo u''qh'urggr ''cr pgc0'Sleep Breath. 4236'O ct ''370']Gr wd''cj gcf ''qh''r tkpv_"
- •Á Cduvtcev'ceegr vgf 'hqt 'r tgugpvcvkqp"cv'EJ GUV'4236Á
 - A Grkeuuqp'CJ.'Meuj cpk'OF.'Fqqf {'OO.'Iqpgu'OM'Xgtperku'OP0Hevki wg'kp'Yqogp'' ku'c'Mg{'U{orvqo'kp'Gxenxevkqp''qh'Urggr'Crpgc0'CHEST.'Qev'4236=Cwuvkp.'VZ0A
- •Á Cduxtcev'uxdo kvgf 'hqt'r tgugpvcvkqp"cv'CJ C"Uekgpvkhke"Uguukqp"4236A
 - A Mcuj cpk'O. 'Grkcuuqp'C. 'Gpi ngt'T. 'Hwngt 'E. 'Xgtpcrku'O 0Rtgj {r gtvgpukqp''eqgz kuvu'' y kj 'EXF 'tkun'hcevqtu0'AHA Scientific Session 20140'P qxgo dgt '42360'
- •Á Cduvtcewi'uwdo kwgf 'hqt'r tgugpvcvlqp"cv'Co gtlecp"Eqngi g"qh'Ectf lqnqi {.'86^{ij} "Cppwcn" Uelgpvlhle "Uguulqp"4237Á
 - A Gpi ngt. 'TL 'Xgtpcnku'O P. 'O co wrc 'MC. 'Drcendwtp''J N. 'Mcuj cpk'O. 'Gruy qtyj 'F NO'' Nkr qr tqvgkp 'Kpuwhp'Tgukuvcpeg''Kpf gz '*NR/KT+'Ej cpi gu'y kj 'Y gki j v'Nquu'Hqmqy kpi ''3'' [gct 'Nqy 'Hcv'Xgi cp'F kgv0'American College of Cardiology, 64th Annual Scientific Session.'O ctej ''36/38.''4237.''Ucp'F kgi q.''EC0'
 - A Mcuj cpk'O. 'Grkcuuqp'C. 'Gpi ngt 'T. 'Vwtpgt'G. 'Vuej kn\/ 'P.'I twpgy crf 'O.'J cng{'L" Hwngt 'E. 'Xkmkpgu'V. 'Xgtpcrku'O 0Rtgf kcdgvgu'T gxgtucn'Wukpi 'c'P qxgn'Eqo r tgj gpukxg'' J gcnj 'O qf gn0'American College of Cardiology, 64th Annual Scientific Session.'' O ctej '36/38.''4237.''Ucp'F kgi q.''EC0'''
- A Cduxtcev'uwdo kwgf 'hqt'r tgugpvcvkqp''cv'CJ C'Gr klNkhguv{ rg'Uekgpvkhke''Uguukqp''4237''
 A Mcuj cpk'O .'Grkcuuqp''C.'Gpi rgt'T.''Hwngt'E.''Xkrnkpgu''V.''Xgtpcrku'O 0'O qf guv'Grgxcvkqp''
 kp''Drqqf 'Rtguuwtg''ku''c'Tgf ''Hrci 'hqt''Ectf kqxcuewrct'F kugcug'Tkun0'AHA Epidem-Lifestyle 2015.'O ctej ''42370'
- Á F gxgnqr o gpv'cpf 'ko r ngo gpvcvkqp''qh'Gzgewkxg'O gf kekpg''Rtqi tco ''cv'tgs wguv'qh''QVUI 0'

Xcnkfcvkqp"qh'y g'KEJ R'Ectfkqxcuewrct 'Tkuri'Ueqtg'"

- •Á Rer gt 'r wdrkuj gf 'kp'' *J of Cardiovasc Nurs*
 - A Mcuj cpk'O. 'Grkcuuqp'C. 'Dckrg{ 'M'Xgtpcrku'O 0'C'u{uvgo cvke''crrtqcej 'kpeqtrqtcvkpi " hco kn{ 'j kuvqt { 'ko rtqxgu'kf gpvkhkecvkqp''qh'ectf kqxcuewrct 'f kugcug'tkun0'J of Cardiovasc Nurs04236''O c { '420']Gr wd''cj gcf ''qh''r tkpv_'''

<u>\ GPKVJ</u> <'T get wkwo gpv'kpkkkcvgf "

I nqdcnfETE'Eqo r ngvkqp"

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- •Á Cduxtcev'uwdo kwgf ''vq ''y g''Co gtkecp'Ectf kqmqi { ''qh'Ectf kqmqi { <''
 - A Gruy qtyj 'F N. 'O co wrc'MC. 'Dreendwtp'J N. 'Gpi ngt'TLO. 'Xgtpcrku'O P 0'Ectf kce'' nkguv{ng'kpvgtxgpvkqpu'f khgtkpi 'kp'f kgvct {'uvtkpi gpe{'ko r tqxg'kpuwrkp'tgukuvcpeg'' y tqwi j 'ej cpi gu'kp'nkr qr tqvgkp'r tqhkrgu0Co gtkecp'Eqmgi g''qh'Ectf kqmi {.'86y '' Cppwcn'Uekgpvkhke'Uguukqp.'O ctej '36/38.''4237.''Ucp'F kgi q.''EC0''''
- •Á Rcr gt "r wdrkuj gf "kp"Circulation: Cardiovascular Genetics<"
 - A Gmuy qtyj 'F N.'Etqhv'F V'It.''Y g{cpf v'L'Uwtyj 'NC.'Drcendwtp'J N.'Dwtng'C.'' J cdgtnqtp'O L'O eF {gt'HC.''Igngo c'I N.'xcp'Ncct'T.'O co wrc'MC.''Xgtpcrku'O P 0' Køvgpukxg'ectf kqxcuewrct'tkunitgf wevkqp'kpf wegu'uwuvckpcdng'ej cpi gu'kp''gzr tguukqp''qh'' i gpgu'cpf 'r cvj y c{u'ko r qtvcpv''vq''xcuewrct'hwpevkqp0'Ekte'Ectf kqxcue'I gpgv'' 4236=9<373/3820'''</p>
- •Á Rcr gt''r tgr ctgf "cpf 'y km'dg'uwdo kwgf "\q"Obesity<"
 - A Gruy qtyj "F N.'O co wc'MC.'Drcendwtp''J N.'O eF {gt''HC.''Lgmgo c'I N.'xcp''Ncct'T.'' Gpi ngt''TL''Xgtpcrku'O P 0Ko r qtvcpeg''qh'uwduvcpvkcn'y gki j v''nuu''hqt''cngtkpi ''i gpg'' gzr tguukqp''f wtkpi ''kpvgpukxg''ectf kqxcuewrct''rkhguv{ng''o qf khkecvkqp0Qdgukx{0'''
- Á Rer gt 'r tgr etgf ''cpf ''y kni'dg 'uwdo kwgf 'hqt 'r wdrkeevkqp<''
 - A O co wc "MC."Xgtpcnku'O P. 'Gmuy qty 'F NOC wtkkqp'htqo 'htguv{ng'o qfkhecvkqp'' r tqi tco u'hqt"ectfkqxcuewrct"tkunitgfwevkqp<i gpfgt'ur gekhe"eqpukfgtcvkqpu"cpf'' r tgfkevqtu0"</p>

O gvcdqnle"cpf "O qngewrct "Dkqmi { "Uwsf kgu"kp"Uwti kecn"Kpvgtxgpvkqpu"hqt "O qtdkf "Qdguks{ "

- •Á Rquvgt 'r tgugpvgf ''cv'vj g'Qdgukv{ ''Uqekgv{ ''o ggvkpi u<''
 - •A Dreendwtp'J N.'O co we'MC.'J cdgtmqtp'O L'Dwtng'C.'UrexkmlG.'Ucpp'P L'O ctng{" MT.'Xgtpcrku'O P.'Gmuy qty 'F NOF khgtgpvkcn'ghgevkzgpguu'qh'rer ctqueqr kecm{/ cf lwuvcdng'i cuvtke''dcpf kpi 'xgtuwu'nkhguv{ng'o qf khecvkqp'hqt'o qf kh{kpi 'r reuo c'' nkr qr tqvgkp'r tqhkrgu0Qdgukv{ "4235<'53^{uvi}Cppwcn'Uekgpvkhe'O ggvkpi .'P qxgo dgt''33/38." 4235.'Cvrepvc.'I C0"

I nqdcn'Rtqhknkpi 'Nqpi/vgto 'Uwf {<"Eqorngvgf 'i gpg"gzrtguukqp"cuuc {u'''

Y kpf dgt 'T gugctej 'Kourkwwg''t cpukkqpgf ''q 'pgy 'Kourkwwkqpcn'T gx kgy 'Dqctf ''

•Á Cmi'r tqvqeqnı'hqt "Vcuni'504. "Vcuni'6. "Vcuni'8. "Vcuni'9. "cpf "Vcuni'. 'y gtg"uwdo kwgf "vq"cpf " cr r tqxgf "d{ "vj g'Ej gucr gcng"KDD0'

Reportable Outcomes

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Published Manuscripts (See Appendix A)/Abstracts:

Gruy qtyj 'F N. 'Etqhz'F V'It. 'Y g{cpf v'L 'Uwty' 'NC. 'Drcendwtp'J N. 'Dwtng'C. 'J cdgtnqtp'O L'' O eF {gt'HC. 'Igngo c'I N. 'xcp'Ncct'T. 'O co wrc'MC. 'Xgtpcrku'O P 0'Køygpukxg''ectf kqxcuewrct''tkum' tgf weykqp'kpf wegu''uwuxckpcdng''ej cpi gu'kp''gzr tguukqp''qh'i gpgu''cpf 'r cyj y c{u'ko r qtvcpv'\q''xcuewrct'' hwpeykqp0'*Circ Cardiovasc Genet.* '4236=9<373/3820 Gr wd''4236''Hgd''430'

Grkcuuqp'C. 'Mcuj cpk'O.'O qf rkp'T.'J qy ctf 'T.'Xgtpcrku'O 0'Hcvki wgf ''qp''Xgpwu.'Urggr { ''qp'' O ctuô I gpf gt ''cpf ''tcekcrif khigtgpegu'kp''u{o r vqo u''qh''urggr ''cr pgc0'*Sleep Breath*0'4236''O ct''370']Gr wd''cj gcf ''qh''r tkpv_''

Mcuj cpk'O.'Grkcuuqp'C.'Dckrg{ 'M.'Xgtpcrku'O 0'C'U{uvgo cvke'Crrtqcej 'kpeqtrqtcvkpi 'Hco kn{" J kuvqt{ 'Kortqxgu'K gpvkhkecvkqp''qh'Ectfkqxcuewrct'F kugcug'Tkun0'J of Cardiovasc Nurs. 4236" O c{ '420*Gr vd''cj gcf ''qh''rtkpv+"''

Y crl{ gt'GO .'Xgtpcrlu'O P .'O qf rlp'TGOlfohnvgpeg''qh'E KO V'cu'c''o qvkxcvqt'hqt'j gcnj 'dgj cxlqt'' ej cpi g'lp'c'j gctv'j gcnj 'r tqi tco 0'*Circ*. 4236=34; «CR3480"

Manuscripts-to be submitted:

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F gegy ke| 'C.'J kemi'O.'O co wrc''MC.'Dwtng'C.'J cdgtnqtp'O L'Rcvpg{'J N.'Xgtpcrku'O P.'' Gruy qty 'F NOUP Ru'cuuqekcvgf 'y kj 'r rcuo c'vtki n{egtkf g'rgxgnu'kphrwgpeg'tgur qpug'f wtkpi '' kpvgpukxg''ectf kqxcuewrct'tkunitgf wevkqp0''

Gmuy qtyj 'F N.'O co wrc''MC.'Drcendwtp'J N.'O eF {gt'HC.'Igmgo c'I N.'xcp''Ncct'T.'Gpi ngt'TL'' Xgtpcnku'O P 0Ko r qtvcpeg''qh'uwduvcpvkcn'y gki j v'nquu'hqt"cnugtkpi 'i gpg''gzr tguukqp'f wtkpi 'kpvgpukxg'' ectf kqxcuewrct''nkhguv{ng''o qf khkecvkqp0Qdgukx{''*vq''dg''uwdo kwgf +0''

Mcuj cpk'O.'Głkcuuqp'C.'O qf rkp'T.'Xgtpcrku'O 0'Ectf kqxcuewret'J gcny "Rtqi tco 'Kpetgcugu'Ugrh/ Głłkece{0"

O cowc'MC. "Xgtpcrku'O P. 'Grnuy qtyj 'F NOC wtkskqp'htqo "Nkhguv{ng'O qf khkecvkqp'Rtqi tcou'hqt" Ectf kqxcuewrct 'T kurd Tgf wevkqp<'I gpf gt 'Ur gekhke "Eqpukf gtcvkqpu'cpf 'Rtgf kevqtu0"

O kngt 'GL 'O co wrc 'MC. 'Ngpi 'N. 'Rkge {ej pc 'O. 'Xgtpcrku'O P. 'Dwecrc 'T. 'Gruy qtyj 'F N0' Ectf kqxcuewrct 'f kugcug'tkunihcevqt 'o qf khecvkqp'f getgcugu'j u/ETR'cpf 'o cetqr j ci g'o ki tcvkqp'' kpj kdkqt { 'hcevqt '*O KH-<'Kphrwgpeg''qh'i gpf gt0''

Ucwo "P U."J cnug{"IH"Y cnt gt"GO."Xgtpcntu"O P 0Gzr mttpi "y g"tqng"cpf "ko r cev"qh"ho kgf " o kpf hwpguu"tckpkpi "kp"ej cpi kpi "f kgv"cpf "gzgtekug"dgj cxkqtu0"

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Conclusions

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Appendix A Rwdrkuj gf 'O cpwuetkr w'

Intensive Cardiovascular Risk Reduction Induces Sustainable Changes in Expression of Genes and Pathways Important to Vascular Function

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- **Background**—Healthy lifestyle changes are thought to mediate cardiovascular disease risk through pathways affecting endothelial function and progression of atherosclerosis; however, the extent, persistence, and clinical significance of molecular change during lifestyle modification are not well known. We examined the effect of a rigorous cardiovascular disease risk reduction program on peripheral blood gene expression profiles in 63 participants and 63 matched controls to characterize molecular responses and identify regulatory pathways important to cardiovascular health.
- *Methods and Results*—Dramatic changes in dietary fat intake (-61%; P<0.001 versus controls) and physical fitness (+34%; P<0.001) led to significant improvements in cardiovascular disease risk factors. Analysis of variance with false discovery rate correction for multiple testing (P<0.05) identified 26 genes after 12 weeks and 143 genes after 52 weeks that were differentially expressed from baseline in participants. Controls showed little change in cardiovascular disease risk factors or gene expression. Quantitative reverse transcription polymerase chain reaction validated differential expression for selected transcripts. Lifestyle modification effectively reduced expression of proinflammatory genes associated with neutrophil activation and molecular pathways important to vascular function, including cytokine production, carbohydrate metabolism, and steroid hormones. Prescription medications did not significantly affect changes in gene expression.
- *Conclusions*—Successful and sustained modulation of gene expression through lifestyle changes may have beneficial effects on the vascular system not apparent from traditional risk factors. Healthy lifestyles may restore homeostasis to the leukocyte transcriptome by downregulating lactoferrin and other genes important in the pathogenesis of atherosclerosis.

Clinical Trial Registration—URL: www.clinicaltrials.gov. Unique identifier: NCT01805492 (*Circ Cardiovasc Genet.* 2014;7:151-160.)

Key Words: cardiovascular diseases ■ gene expression ■ lifestyle ■ obesity

Cardiovascular disease (CVD) remains the leading cause of death and healthcare burden in the United States, accounting for 1 of every 3 deaths and \approx \$313 billion in healthcare-related costs in 2009.¹ Many patients with coronary artery disease (CAD) require expensive surgical interventions, such as coronary artery bypass grafting or percutaneous catheter placement, with significant morbidity and mortality.²

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Abundant research has established the relationship between dietary habits and CVD risk,^{3,4} and physical activity has been associated with significant reductions in cardiac mortality.⁵ Lifestyle modification programs focusing on nutrition and exercise have shown substantial health benefits,⁶ in part, by improving endothelial function, reducing cardiovascular events, and slowing or reversing progression of coronary

atherosclerosis.⁷ Although lifestyle programs are effective in mediating CVD risk through traditional risk factors, little is known about molecular change during intensive lifestyle modification or the significance of molecular responses in long-term CVD risk reduction.

We report the effect of an intensive lifestyle program on peripheral blood gene expression to improve our understanding of cellular and molecular changes that occur during risk reduction in patients with, or at risk for, heart disease. Previous studies have shown that patterns of gene expression in peripheral blood are associated with various CVD phenotypes, including presence of CAD⁸ and extent of coronary artery atherosclerosis.^{9,10} Our study reveals that gene expression signatures are significantly modulated by rigorous lifestyle behaviors and track with CVD risk profiles over time. These observations suggest that successful and sustained

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Circ Cardiovasc Genet is available at http://circgenetics.ahajournals.org

modulation of gene expression through lifestyle changes may have beneficial effects on vascular health that cannot be discerned from traditional risk factor profiles.

Methods

Participants

The research protocol was approved by the Institutional Review Board at Windber Medical Center. All subjects volunteered to participate and gave written informed consent. Men and women willing to make comprehensive lifestyle changes completed a prospective, nonrandomized clinical intervention to stabilize or reverse progression of heart disease through changes in lifestyle. Entry criteria were (1) diagnosis of CAD, which included stable angina, angioplasty, evidence of \geq 50% luminal narrowing on coronary angiogram, acute myocardial infarction, bypass surgery, or stent placement; or (2) \geq 2 CAD risk factors: hypertension (systolic pressure >140 mm Hg or diastolic pressure >90 mm Hg), high total cholesterol (>200 mg/dL), diabetes mellitus, obesity defined as body mass index (BMI) \geq 30, or family history of heart disease in parents or siblings. Controls receiving only standard care from their primary physicians were prospectively matched to program participants based on age, sex, and disease status.¹¹

Traditional CAD Risk Factors and Diet

Participants were enrolled on an ongoing basis in a lifestyle intervention that consisted of 4 components: (1) low-fat vegetarian diet (<10% of calories from fat), (2) 180 minutes/wk of moderate aerobic exercise, (3) 1 hour of stress management each day, and (4) weekly group support sessions. Demographic and clinical information was obtained by standard questionnaires at baseline, 12 weeks, and 52 weeks. Physiological and biochemical variables were assessed as previously described.^{12,13} Dietary data were collected from self-reported 72-hour dietary recall questionnaires. Food Processor v8.4.0 (ESHA Research) was used to determine daily caloric intake and nutrient composition.

Blood Collection, RNA Preparation, and Microarray Analysis

Peripheral blood was obtained from participants at each time point using the PAXgene Blood RNA System (Qiagen). RNA was isolated and quantified following the Qiagen protocol. Globin mRNA transcripts were depleted from a portion of each total RNA sample using the GLOBINclear-Human kit (Ambion). Globin-depleted RNA aliquots (1 µg) were amplified using the MessageAmp II aRNA Amplification System (Ambion). Resulting double-stranded cDNA was purified, amplified, and labeled with biotin-11-uridine-5'triphosphate. Labeled aRNA (15 µg) was then fragmented and hybridized to GeneChip Human Genome U133A 2.0 arrays (Affymetrix) and scanned on a GeneChip Scanner 3000. Samples were run in batches for globin reduction (n=12), RNA amplification (n=12), and microarray analysis (n=6), keeping all 3 time points for each participant together in the same batch to minimize technical artifact. All gene expression data have been deposited in the Gene Expression Omnibus, series accession number GSE46097 (http://www.ncbi.nlm. nih.gov/geo/query/acc.cgi?acc=GSE46097).

Informatics and Analysis

Statistical analysis of CVD risk factors was conducted using JMP (v9.0). Baseline levels for intervention and matched controls were compared using a matched pairs t test, and change in risk factors over time was assessed with a Wilcoxon signed-rank test, which analyzed differences in risk factor response among the matched pairs.

Partek Genomics Suite v6.5 (Partek Incorporated) was used to analyze gene expression data from the 378 CEL files, which all passed standard quality control assessment. Duplicate blood samples collected at each time point from 7 random participants indicated high repeatability of the microarray data (average Pearson correlation of normalized intensities was 0.992 ± 0.006 ; range, 0.969-0.996). Paired *t* tests identified 9 genes that were excluded from further analysis

because of significant differences in expression among duplicate samples (Table I in the Data Supplement).

Using 1-way analysis of variance with false discovery rate correction for multiple testing, we first compared baseline levels of gene expression between lifestyle participants and controls and then examined expression changes from baseline to week 12 and baseline to week 52 in lifestyle participants, and separately in controls, to determine genes that changed significantly over time in each group. Stringent gene lists were generated through combined significance (FDR P<0.05) and expression change (≥1.1-fold) filtering. Pairwise Pearson productmoment correlations between changes in gene expression and changes in CVD risk factors were calculated using JMP. Functional enrichment analysis was performed on stringent gene lists to identify biological processes controlled by differentially expressed genes. Gene set enrichment analysis, using BRB-ArrayTools v4.2.1 on the Kyoto Encyclopedia of Genes and Genomes database, identified differential expression between groups of genes with common biological function or regulation.¹⁴ To distinguish the effects of the program from the potential influence of medications on gene expression, ancillary analyses were conducted that included only participants who were not taking or did not change the brand or dosage of medications in the following categories: angiotensin-converting enzyme inhibitors, β-blockers, calcium channel blockers, or lipid-lowering drugs.

Transcript Validation by Quantitative Reverse Transcription Polymerase Chain Reaction

Total RNA (500 ng) was reverse transcribed using the High-Capacity cDNA Reverse Transcription Kit (Applied Biosystems) and subjected to quantitative reverse transcription polymerase chain reaction using TaqMan Gene Expression Assays (Applied Biosystems). All target gene expression levels were normalized to the housekeeping gene GAPDH. Samples were run in duplicate for each assay, and the mean value was analyzed by the $\Delta\Delta C_T$ method.^{15,16} A repeated measures analysis of variance then determined whether fold-change in expression between time points for each gene was statistically significant. Additional materials and methods are described in the Data Supplement.

Results

The average age of lifestyle participants was 60.3 years (range, 44.5–78.4 years). Many participants entered the program with clinically relevant disorders: 41% had hypertension, 60% were clinically obese, and 54% had high cholesterol. At baseline, participants had higher average BMI (32.6 ± 6.7 versus 28.4 ±3.9) and triglycerides (187 ± 101 versus 133 ± 73 mg/dL) but lower exercise capacity (24.9 ± 7.4 versus 36.7 ± 11.9 mL per kg per minute) than controls (P<0.01), despite the prospective matching strategy (Table II in the Data Supplement). Participants who completed the program tended to be older (60.3 ± 9.3 versus 55.3 ± 11.3 years of age) and have higher systolic blood pressure (137 ± 17 versus 131 ± 19 mmHg) than those who dropped out (P<0.05; Table III in the Data Supplement).

Traditional CAD Risk Factors and Diet

The program resulted in substantial reductions in the number of hypertensive (41% down to 17%), obese (60%–37%), and dyslipidemic (54%–37%) patients. In the first 12 weeks, participants showed dramatic improvement in most dietary and CVD risk factors, but little change occurred in controls (Table 1). At 52 weeks, participants maintained significantly lower daily fat intake (–60%; P<0.001 compared with matched controls) and higher carbohydrate consumption (+30%; P<0.001 versus matched controls). Improvements in BMI (–9%; P<0.001), triglycerides (–7%; P<0.01), and physical fitness (+38%; P<0.001) remained significant compared with matched nonintervention

Controls (n=63)					Participants (n=63)				
Measure	Baseline	12 Weeks	52 Weeks	% Change B-W52*	Baseline	12 Weeks	52 Weeks	% Change B-W52*	Matched Pairs <i>P</i> †
Dietary									
Calories	1750±547	1719±591	1633±462	-6.7	1985±763	1505±293‡	1700±442§	-14.4	0.369
% Carbohydrate	49.3±10.0	49.3±7.3	49.9±10.1	+1.2	54.5±10.8	71.2±3.8‡	71.1±3.6‡	+30.4	< 0.001
% Fat	32.4±9.3	32.6±6.3	31.7±8.2	-2.2	29.1±10.3	11.2±1.9‡	11.4±3.0‡	-60.7	< 0.001
Physiological									
BMI, kg/m²∥	28.4±3.9	28.1±4.1	28.6±4.2	+0.8	32.6±6.7	30.2±6.1‡	29.6±6.2‡	-9.4	<0.001
SBP, mmHg	134±18	128±15§	126±13‡	-5.7	139±16	124±16‡	129±17‡	-7.6	0.277
DBP, mmHg	79.3±10.3	77.7±8.6	77.4±8.2	-2.4	82.2±9.9	73.5±8.8‡	76.2±9.2‡	-7.3	0.064
LDL, mg/dL	111±36	107±34	110±36	-1.5	116±42	101±33‡	114±35	-1.3	0.958
TCH, mg/dL	192±46	189±45	190±46	-1.1	200±49	173±42‡	192±43§	-3.9	0.207
TG, mg/dL∥	133±73	151±146	145±77	+8.6	187±101	168±82	174±102	-7.0	0.005
EC (Vo ₂ max)II	36.5±11.8	37.5±11.2	36.4±11.1	-0.1	25.0±8.0	32.0±8.3‡	34.6±10.0‡	+38.4	<0.001

Table 1.	Change in Dietary a	nd Cardiovascular Risk	Factors in Participants	and Controls
	······································			

Data presented as mean±SD. There were 36 women and 27 men in each group; 3.7% missing data. BMI indicates body mass index; DBP, diastolic blood pressure; EC, exercise capacity; LDL, low-density lipoprotein; SBP, systolic blood pressure; TCH, total cholesterol; and TG, triglycerides.

*Percent change from baseline to 52 wk.

+From a Wilcoxon signed-rank test for matched pairs comparing changes from baseline to 52 wk in participants and matched controls.

 $\pm P < 0.001$ compared with baseline by a paired *t* test.

P<0.05 compared with baseline by a paired *t* test.

Baseline values significantly different (*P*<0.05) between participants and controls based on a matched pairs *t* test.

controls, but systolic blood pressure and lipids showed regression toward pretreatment levels.

Gene Expression

Levels of gene expression were similar between participants and controls at baseline—only 1 (214731_at) of 22277 probes showed a significant difference (FDR *P*<0.05) between groups. Stringent differential analysis identified 26 unique genes (3 upregulated and 23 downregulated) that changed significantly in expression after 3 months of intervention (Table IV in the Data Supplement). By 1 year, 143 characterized genes were significantly upregulated (n=44) or downregulated (n=99) from baseline in lifestyle participants (Table 2; Table V in the Data Supplement). Downregulation of gene expression during lifestyle change occurred far more frequently than expected by chance. Using a binomial distribution calculated as a probability mass function with P=0.5, the probability was 3.9×10^{-5} for observing 23 of 26 genes downregulated at 12 weeks and 1.4×10⁻⁶ for 99 of 143 genes downregulated at 52 weeks. Validation using quantitative reverse transcription polymerase chain reaction confirmed the overall accuracy of the array-based expression results for the transcripts tested (Table 3). In contrast to lifestyle participants, control subjects showed no change in gene expression after 12 weeks (0 genes) and little change by 52 weeks (21 genes; Table VI in the Data Supplement).

Correlations Between CVD Risk Factors and Gene Expression

Throughout the program, many genes exhibiting the largest fold-changes in expression were significantly correlated with BMI (Figure 1). Notably, few genes correlated with blood pressure or plasma lipids after 12 weeks. Dysregulation of several genes was associated with improvement in triglycerides (-10%)

during the first 3 months but was not associated after the 12-week examination when triglyceride levels regressed toward baseline.

Functional Analysis

Functional enrichment analysis indicated that genes showing significant changes in expression during the intervention function mainly in immune response and cholesterol storage (Table VII in the Data Supplement). Genes with the greatest changes in expression at 12 weeks showed regression by 52 weeks (Figure 2). Expression of the majority of immune response genes (65%) closely paralleled the substantial improvement followed by regression pattern observed for some traditional risk factors. In contrast, many cholesterol/lipid homeostasis genes (67%) showed a pattern of continual change throughout the program similar to BMI.

Gene set enrichment analysis provided additional insight into molecular pathways regulated by cardiovascular risk factor modification but that were subtle at the individual gene level. Table 4 shows Kyoto Encyclopedia of Genes and Genomes pathways with Efron–Tibshirani max mean statistic¹⁷ ≤0.001 at 12 and 52 weeks. Pathways affected early in lifestyle modification were related to carbohydrate metabolism, glycoprotein hormone levels, and cytokine production, whereas pathways altered later control steroid hormones, cell mobility, and signal transduction and inflammation.

Effects of Medications

Participants were taking 79 different prescription medications at baseline. To determine whether common cardiovascular medications affected gene expression, we examined subgroups of participants based on medication use. In these analyses, changes in expression in participants not taking cardiovascular medications or whose medication levels did not change during

Probe ID	Gene Name	Symbol	Fold-Change	Gene Ontology Biological Process*
202018_s_at†	Lactotransferrin	LTF	-1.67	Immune response, ion transport, iron homeostasis
221748_s_at	Tensin 1‡	TNS1	-1.55	Cell migration, cell-substrate junction assembly
212531_at†	Lipocalin-2	LCN2	-1.47	Transporter activity; binding§
206676_at†	Carcinoembryonic antigen-related CAM8	CEACAM8	-1.44	Immune response
214407_x_at	Glycophorin B (MNS blood group)‡	GYPB	-1.41	Signal transduction; receptor activity§
206698_at	X-linked Kx blood group	XK	-1.41	Amino acid transport
206665_s_at	BCL2-like 1	BCL2L1	-1.39	Response to hypoxia/oxidative stress, apoptosis
203502_at	2,3-bisphosphoglycerate mutase	BPGM	-1.37	Carbohydrate metabolism, glycolysis, respiration
203115_at	Ferrochelatase‡	FECH	-1.35	Cholesterol metabolism, metabolites/energy
207802_at†	Cysteine-rich secretory protein 3	CRISP3	-1.32	Immune response, defense response
208470_s_at†	Haptoglobin/haptoglobin-related protein‡	HP/HPR	-1.30	Defense response, proteolysis, iron homeostasis
212768_s_at†	Olfactomedin 4	OLFM4	-1.29	Cell adhesion, protein binding
213446_s_at	IQ motif containing GTPase-activating protein 1‡	IQGAP1	-1.28	Small GTPase-mediated signal transduction
208632_at	Ring finger protein 10	RNF10	-1.28	Transcription, Schwann cell proliferation
221627_at	Tripartite motif containing 10	TRIM10	-1.28	Erythrocyte differentiation; protein/ion binding§
218418_s_at	KN motif and ankyrin repeat domains 2	KANK2	-1.28	Transcription apoptosis, cell proliferation
217878_s_at	Cell division cycle 27 homolog‡	CDC27	-1.27	Cell proliferation, cell division
210244_at†	Cathelicidin antimicrobial peptide	CAMP	-1.27	Defense response
200615_s_at	Adaptor-related protein complex 2, β 1	AP2B1	-1.26	Protein transport, defense response
205557_at†	Bactericidal/permeability-increasing protein	BPI	-1.25	Immune response; lipid binding§
211993_at	WNK lysine-deficient protein kinase 1	WNK1	-1.25	BP regulation, phosphorylation, ion transport

Table 2. Genes Showing Greatest Fold-Change in Expression During CVD Risk Factor Modification

Stringent gene list of changes at 52 wk with combined significance (FDR P<0.05) and expression change (≥1.25-fold) filtering. BCL2 indicates B-cell CLL/lymphoma 2; BP, blood pressure; CAM, cell adhesion molecule; and CVD, cardiovascular disease.

*Derived from NetAffx Analysis Center (http://www.affymetrix.com/analysis/index.affx).

†Probes were significant at 12 wk.

*Three probes for TNS1 and GYPB and 2 probes for FECH, HP/HPR, IQGAP, and CDC27 showed a significant fold-change from baseline to 52 wk. §Gene Ontology molecular function.

the study were similar to changes in all participants, showing that prescription medication use did not have significant effects on gene expression during lifestyle change (Table 5).

Discussion

Participants who completed a comprehensive lifestyle intervention designed to reverse or stabilize progression of CAD dramatically changed their dietary habits and significantly increased physical activity, which led to substantial weight loss during 1 year. We have previously shown that CVD risk reduction through intensive lifestyle change has positive effects on vascular and mental health by reducing cardiometabolic risk,12 modulating plasma lipoprotein profiles,13 and improving clinical measures of depression and stress.¹⁸ Here, we show that

Table 3	Validation of Differential	Gene Expression	During CVD Ris	k Factor Modification
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		Controls	(n=45)						
Gene	12-Week Fold-Change	P Value*	52-Week Fold-Change	P Value†	12-Week Fold-Change	P Value*	52-Week Fold-Change	P Value†	Time×CS-CN <i>P</i> Value‡
LTF	+0.67	0.469	+0.89	0.328	-2.01	0.002	-1.72	0.026	0.037
LCN2	+0.58	0.202	+0.62	0.187	-0.91	0.078	-0.98	0.057	0.020
CEACAM8	+1.11	0.274	+1.22	0.279	-3.44	0.006	-1.75	0.049	0.010
CRISP3	+1.02	0.230	+1.28	0.242	-2.35	0.005	-1.56	0.004	0.007
HP	+0.15	0.484	-0.07	0.983	-0.96	0.007	-1.18	<0.001	0.008
OLFM4	+1.87	0.102	-0.30	0.625	-6.97	0.011	-4.56	0.071	0.026
CAMP	+0.44	0.230	+0.07	0.562	-1.10	0.007	-1.32	0.033	0.012
BPI	+0.16	0.519	-0.17	0.914	-1.18	0.017	-0.81	0.044	0.040

Validation using quantitative reverse transcription polymerase chain reaction and the $\Delta\Delta C_{-}$ method was conducted on 45 controls and 44 participants with sufficient RNA remaining for analysis. CVD indicates cardiovascular disease; CN, controls; and CS, cases (or participants).

*P value comparing 12 wk to baseline using a paired t test.

†P value comparing 52 wk to baseline using a paired *t* test.

#Between-group P value for time variable using a repeated measures analysis of variance comparing program participants (CS) with controls (CN).

D W12	BMI	SBP	DBP	LDL	TCH	TG	EC
B-W12	-7.5%	-11.1%	-10.7%	-12.9%	-13.4%	-10.1%	+28.1%
LTE	10.44	.0.12	10.19	10.22	10.22	10.11	0.00
LIF TNS1	+0.44	+0.12	+0.18 ±0.05	+0.23	+0.23	+0.11	+0.09
LCN2	± 0.32	+0.01	+0.03	+0.00	+0.09	+0.08	-0.01
CEACAM8	+0.47	+0.06	+0.03	+0.32	+0.26	+0.09	-0.03
GYPB	+0.04	-0.04	-0.05	-0.05	-0.10	-0.11	+0.13
XK	+0.04	-0.02	-0.02	-0.03	-0.09	-0.18	+0.17
BCL2L1	-0.04	+0.03	+0.07	-0.06	-0.15	-0.27	+0.10
BPGM	+0.10	-0.06	+0.01	-0.01	-0.05	-0.11	+0.18
FECH	+0.09	-0.04	+0.01	-0.12	-0.15	-0.12	+0.12
CRISP3	+0.41	+0.02	+0.06	+0.21	+0.28	+0.27	-0.14
HP/HPK	+0.32	+0.07	+0.24	+0.22	+0.24	+0.01	-0.01
IOGAP1	± 0.03	+0.02	± 0.03	+0.29 +0.04	-0.02	+0.20	+0.00
RNF10	+0.07	-0.03	+0.04	-0.09	-0.19	-0.26	+0.05
TRIM10	+0.05	-0.06	-0.05	-0.06	-0.16	-0.25	+0.10
KANK2	-0.01	-0.07	-0.01	-0.12	-0.20	-0.19	+0.09
CDC27	+0.05	-0.10	+0.01	-0.10	-0.15	-0.26	-0.07
CAMP	+0.29	0.00	+0.04	+0.13	+0.18	+0.17	-0.01
AP2B1	+0.07	-0.09	+0.15	+0.02	-0.09	-0.27	+0.07
BPI	+0.34	+0.21	+0.17	+0.10	+0.07	-0.02	+0.03
WNK1	+0.01	-0.03	+0.03	-0.12	-0.19	-0.25	+0.09
	DM	ODD	DDD	IDI	TOU	TO	ГC
W12 52	BWI	SRL	DRA	LDL	TCH	TG	EC
W 12-32	-2.0%	+4.0%	+3.8%	+13.3%	+11.1%	+3.4%	+8.0%
LTE	+0.24	+0.12	+0.06	0.10	0.11	+0.23	0.26
TNS1	+0.24	+0.12	+0.00	-0.19	_0.09	+0.11	-0.20
LCN2	+0.39	+0.11	+0.05	-0.23	-0.19	+0.07	-0.32
CEACAM8	+0.27	+0.06	+0.01	-0.18	-0.14	+0.15	-0.26
GYPB	+0.50	+0.07	+0.03	-0.24	-0.22	0.00	-0.39
XK		+0.06	-0.01	-0.22	-0.22	-0.02	-0.36
BCL2L1	+0.33	+0.05	-0.03	-0.07	-0.06	+0.02	-0.31
BPGM	+0.49	+0.03	-0.05	-0.20	-0.18	-0.01	-0.35
FECH	+0.48	+0.09	-0.01	-0.18	-0.18	-0.01	-0.37
CRISP3	+0.26	-0.08	-0.05	-0.22	-0.20	+0.08	-0.18
OL FM4	+0.32	-0.05	-0.03	-0.52	-0.27	+0.09	-0.18
IOGAP1	0.00	+0.01	+0.18	+0.10	+0.11	+0.14	-0.03
RNF10	+0.29	+0.12	+0.04	-0.16	-0.12	+0.09	-0.33
TRIM10	+0.36	+0.07	-0.02	-0.21	-0.20	+0.02	-0.38
KANK2	+0.37	+0.08	-0.09	-0.12	-0.12	-0.02	-0.35
CDC27	+0.13	+0.12	+0.04	-0.03	-0.01	+0.05	-0.32
CAMP	+0.34	+0.02	+0.03	-0.31	-0.29	-0.02	-0.29
AP2B1	+0.26	+0.08	-0.05	-0.08	-0.04	+0.15	-0.29
BPI	+0.25	+0.17	+0.08	-0.29	-0.27	+0.02	-0.24
WINKI	+0.14	+0.10	0.00	+0.03	+0.07	+0.18	-0.17
	DM	CDD	DDD	IDI	TOU	тa	ГC
B-W52	BIM	SPL	DRA	LDL	ICH	10	EC
D -W 52	-9.4%	-7.6%	-7.3%	-1.3%	-3.9%	-7.0%	+38.4%
LTE	+0.46	+0.16	+0.08	+0.18	+0.25	+0.14	-0.35
TNS1	+0.38	+0.13	+0.01	+0.05	+0.08	+0.01	-0.26
LCN2	+0.34	+0.20	+0.05	+0.15	+0.16	+0.08	-0.30
CEACAM8	+0.38	+0.10	+0.07	+0.32	+0.33	+0.06	-0.30
GYPB	+0.39	+0.14	+0.05	0.00	-0.02	-0.04	-0.25
XK	+0.32	+0.12	+0.09	+0.07	+0.05	-0.11	-0.20
BCL2L1	+0.18	+0.10	-0.12	+0.08	+0.06	-0.06	-0.21
BPGM	+0.35	+0.11	+0.10	+0.09	+0.07	-0.13	-0.21
CRISP3	+0.32	_0.02	+0.01	+0.08	+0.07	+0.12	-0.18
HP/HPR	+0.46	+0.01	+0.25	+0.14	+0.04	-0.11	-0.10
OLFM4	+0.35	-0.02	+0.06	+0.15	+0.14	+0.02	-0.18
IQGAP1	+0.20	+0.12	+0.04	+0.02	+0.01	0.00	-0.33
RNF10	+0.38	+0.10	-0.05	+0.02	+0.05	+0.03	-0.29
TRIM10	+0.35	+0.12	0.00	0.00	0.00	-0.10	-0.22
KANK2	+0.32	+0.09	-0.10	+0.02	+0.02	-0.12	-0.21
CDC27	+0.11	-0.02	-0.11	-0.16	-0.16	-0.01	-0.28
CAMP	+0.37	+0.15	+0.21	+0.17	+0.16	+0.04	-0.10
AP2B1	+0.41	+0.07	+0.13	+0.04	+0.05	-0.05	-0.20
BLI	+0.29	+0.23	+0.17	+0.24	+0.19	-0.07	-0.18

Figure 1. Pairwise correlations for changes in cardiovascular disease risk factors and gene expression from baseline to 12 weeks (top), week 12 to week 52 (middle), and baseline to week 52 (bottom) during intensive lifestyle modification. Percentages in column headings represent degree of change for each risk factor during the corresponding time interval. Coefficients highlighted in dark green were significant at P<0.001, light green P<0.05. Risk factor percent changes are group averages from Table 1; changes in gene expression were calculated as a percent change for each gene at week 12 and week 52 using raw expression data. Stringent gene list of changes at 52 weeks with combined significance (FDR P<0.05) and expression change (\geq 1.25-fold) filtering. BMI indicates body mass index; DBP, diastolic blood pressure; EC, exercise capacity; LDL, low-density lipoprotein; SBP, systolic blood pressure; TCH, total cholesterol; and TG, trialvcerides.



Figure 2. Changes in cardiovascular disease (CVD) risk factors (top) and levels of expression for genes differentially regulated during intensive CVD risk reduction (bottom). Blue lines, FDR P<0.05 and fold-change \geq 1.1 but <1.25; red lines, FDR P<0.05 and fold-change \geq 1.25 at 52 weeks. BMI indicates body mass index; DBP, diastolic blood pressure; EC, exercise capacity; LDL, low-density lipoprotein; SBP, systolic blood pressure; TCH, total cholesterol; and TG, triglycerides.

intensive lifestyle behaviors also modulate gene expression in peripheral blood, suggesting potential CVD risk-reduction mechanisms involving leukocyte function in innate immunity, lipid homeostasis, and inflammation.

Lifestyle modification has been shown to be effective in improving clinically relevant CVD risk factors; however, the extent, persistence, and significance of molecular change accompanying CVD risk reduction are not well known. Daily macronutrients can influence short-term changes in genes related to inflammation, carbohydrate metabolism, and immune function,¹⁹ whereas long-term dietary composition may affect genes and pathways regulating development of atherosclerosis and CVD.²⁰ Similarly, physical activity induces a variety of rapid biophysical and biochemical responses, including altered expression of genes related to oxidative stress, signal transduction, and inflammation.^{21,22} Because expression of diet- and exercise-responsive genes tends to be transient in nature, little is known about the long-term clinical significance of these changes.

During lifestyle modification, participants successfully adopted healthy lifestyle behaviors including a low-fat diet and increased physical activity, which may be important drivers of molecular change. In our analysis of individual

ID	Name	No. Genes	Function
Baseline: wk 12			
hsa05120	Epithelial cell signaling in Hpy infection	53	Gene expression and proinflammatory cytokine production in gastric mucosa
hsa04912	GnRH signaling pathway	64	Synthesis/release of gonadotropins; gene expression, stress response
hsa00640	Propanoate metabolism	26	Carboxylic acid metabolism; related to carbohydrate metabolism/glycolysis
Baseline: wk 52			
hsa00150	Androgen and estrogen metabolism	19	Inactivation/catabolism of androgen and estrogen in target tissues
hsa00563	GPI anchor biosynthesis	18	Covalently anchor proteins to cell membranes; signal transduction, inflammation
hsa04810	Regulation of actin cytoskeleton	136	Cellular processes associated with membrane dynamics, cell migration/motility

Table 4. KF	EGG Pathwa	s Differentially	/ Ex	pressed	During	CVD	Risk	Factor	Modification
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The Efron–Tibshirani max mean statistic for all pathways was ≤ 0.001 . Available at http://www.genome.jp/kegg/pathway.html. Only galactose metabolism and calcium signaling pathways were differentially expressed in controls at 52 wk. CVD indicates cardiovascular disease; GnRH, gonadotropin-releasing hormone; GPI, glycosylphosphatidylinositol; Hpy, *Helicobacter pylori*; and KEGG, Kyoto Encyclopedia of Genes and Genomes.

genes, immune response and lipid homeostasis were enriched functional categories. The drastic reduction in dietary fat intake during the intervention may influence expression of genes related to lipid storage and transport. Similarly, the predominant downregulation of immune/defense response genes may reflect lower psychological stress and improved vascular health. Single-gene analysis may miss important effects of lifestyle change on complex molecular pathways; therefore, we conducted gene set enrichment analysis to overview biological processes relevant to CVD risk reduction. Pathways significantly altered were related to physiological changes during the program. The gonadotropin-releasing hormone signaling pathway and the androgen and estrogen metabolism pathway

Table 5. Effects of Medications on Gene Expression From Baseline to 52 Weeks

		Fold-Change	Fold-Change With Stable or No Lipid	Fold-Change With Stable or No CVD	Among
		All Participants	Medications	Medications	Group
Probe ID	Symbol	(n=63)	(n=51)*	(n=34)†	<i>P</i> ‡
202018_s_at	LTF	-1.67	-1.67	-1.70	0.988
221748_s_at	TNS1	-1.55	-1.51	-1.43	0.953
212531_at	LCN2	-1.47	-1.44	-1.48	0.978
206676_at	CEACAM8	-1.44	-1.48	-1.68	0.368
214407_x_at	GYPB	-1.41	-1.34	-1.26	0.768
206698_at	XK	-1.41	-1.43	-1.36	0.933
206665_s_at	BCL2L1	-1.39	-1.35	-1.31	0.946
203502_at	BPGM	-1.37	-1.40	-1.41	0.961
203115_at	FECH	-1.35	-1.31	-1.28	0.933
207802_at	CRISP3	-1.32	-1.32	-1.43	0.637
208470_s_at	HP/HPR	-1.30	-1.31	-1.24	0.856
212768_s_at	OLFM4	-1.29	-1.20	-1.23	0.540
213446_s_at	IQGAP1	-1.28	-1.25	-1.22	0.951
208632_at	RNF10	-1.28	-1.25	-1.18	0.803
221627_at	TRIM10	-1.28	-1.23	-1.21	0.811
218418_s_at	KANK2	-1.28	-1.22	-1.21	0.890
217878_s_at	CDC27	-1.27	-1.26	-1.22	0.961
210244_at	CAMP	-1.27	-1.26	-1.27	0.996
200615_s_at	AP2B1	-1.26	-1.24	-1.22	0.961
205557_at	BPI	-1.25	-1.22	-1.29	0.723
211993_at	WNK1	-1.25	-1.23	-1.17	0.860

CVD indicates cardiovascular disease.

*Includes only participants not taking lipid-lowering medications or whose lipid-lowering medication levels did not change during the study.

 \pm threshold the taking angiotensin-converting enzyme inhibitors, β -blockers, calcium channel blockers, or lipid-lowering medications or whose medication levels for these drugs did not change during the study.

+Based on a Kruskal–Wallis nonparametric test comparing change in gene expression from baseline to 52 wk among groups. regulate steroid hormones and activate diverse signaling pathways in nonpituitary tissues that modulate gene expression, cell proliferation, and stress response.²³ Because estrogen and androgen levels are commonly elevated in obesity and weight loss can significantly lower serum estrogen and testosterone levels,²⁴ weight reduction may lead to changes in pathways affecting sex hormones. Similarly, the propanoate metabolism pathway is related to carbohydrate metabolism and glycolysis; thus, functional changes may reflect increased carbohydrate consumption during the program.

The *Helicobacter pylori* bacterium colonizes the human gastric mucosa and activates multiple signaling pathways.²⁵ Weight loss through dietary change has been shown to significantly alter the species composition of the intestinal microbiome,²⁶ thus activation of the *H. pylori* pathway in the first 12 weeks may reflect changes in gut microbiota because of significant dietary changes. Other pathways involving the actin cytoskeleton and glycosylphosphatidylinositol anchor biosynthesis are related to signal transduction, inflammation, and host–pathogen interactions.²⁷

Whole blood RNA isolation systems such as PAXgene accurately capture in vivo transcription profiles but cannot distinguish expression signatures unique to specific cell types. To better understand vascular responses to lifestyle modification, we compared genes that were differentially regulated during CVD risk reduction to expression signatures reported for major leukocyte subpopulations. Genes influenced by lifestyle change were expressed in several cell populations, suggesting that different types of circulating cells with unique and specialized functions may be involved in vascular responses to lifestyle modification (Figure 3).

Neutrophils and T-lymphocytes comprise the most abundant leukocyte populations and play essential roles in inflammation and microbial infection. Genes expressed by these specialized cells were downregulated during lifestyle modification, which provides insight into their vascular function and potential role in mediating cardiovascular risk. In particular, neutrophil lactoferrin (LTF; or lactotransferrin) is a multifunctional glycoprotein that serves an important role in host defense and innate immunity. In the circulatory system, LTF



Figure 3. Congruence between cardiovascular disease (CVD) risk-reduction genes and expression signatures reported for major leukocyte subpopulations or CVD-relevant processes. Squares denote whether genes differentially regulated after 52 weeks of intensive lifestyle modification also were expressed (green squares) or not expressed (red squares) in published profiles. *Palmer et al²⁸; †Whitney et al²⁹; ‡Cobb et al³⁰; §Wang et al³¹; ||Calvano et al.³²; #Xiao et al.³³

released by neutrophils regulates production of reactive oxygen species, recruits immune cells to sites of inflammation, and is positively associated with coronary artery stenosis³⁴ and risk for fatal ischemic heart disease.35 LTF gene expression is induced in atherosclerotic plaques of human aortas compared with nonatherosclerotic internal thoracic arteries,³⁶ and salivary LTF concentrations are 60% lower in elite athletes versus sedentary controls.37 Importantly, in vitro studies have shown that LTF directly affects leukocyte functions that contribute to CVD, including attenuating leukocyte adhesion to vascular endothelial cells, modulating proinflammatory cytokine expression in endothelial cells, and inhibiting processes essential for vascular dysfunction such as proliferation, migration, and angiogenesis.³⁸ Such parallel evidence implicating LTF in vascular health increases confidence in the validity of our findings and suggests LTF may be therapeutic in patients with CVD who lead unhealthy lifestyles.

Lipocalin-2 (or neutrophil gelatinase-associated lipocalin) is a proinflammatory glycoprotein released by activated neutrophils in response to inflammatory stimuli.³⁹ Clinical and experimental studies suggest serum lipocalin-2 levels are elevated in obesity and related metabolic complications⁴⁰ and positively associated with CAD and cardiac dysfunction.41,42 Lipocalin-2 is highly expressed in vascular smooth muscle cells and may function in atherosclerotic plaque development by promoting endothelial activation and vascular leukocyte infiltration.43 Carcinoembryonic antigen-related cell adhesion molecules are immunoglobulin-related glycoproteins that are glycosylphosphatidylinositol-anchored to the surface of granulocytes (neutrophils and eosinophils), where they regulate activation and release of proinflammatory mediators during inflammation and host immunity.44 Carcinoembryonic antigen-related cell adhesion molecules have been shown to influence neutrophil adhesion to human umbilical vein endothelial cells.45

Changes in blood leukocyte gene expression when immune cell function is accentuated, such as systemic inflammation and severe trauma, provide further insight into regulation of leukocyte function during CVD risk reduction. In response to severe bodily injury and infection, leukocytes significantly upregulate expression of numerous genes involved in inflammation and innate immunity.^{32,33} Interestingly, genes showing some of the greatest fold increases in expression during severe trauma (LTF, matrix metallopeptidase 8, and haptoglobin) were significantly downregulated during lifestyle change. Lifestyle modification thus may have beneficial effects on vascular health by reducing expression of proinflammatory genes associated with activation of neutrophil granulocytes.

In this study, we controlled for many covariates known to influence blood-based gene expression profiles,^{29,46} such as age, sex, time of day, and fasting status, through matching and experimental design. Another complicating factor common among patients with CVD is medication use. Many participants entered the program in poor cardiovascular health, with hypertension, obesity, and hyperlipidemia and, as a result, were taking several prescription medications. These medications may affect cellular function and alter patterns of gene expression in peripheral blood,⁴⁷ thus confounding the true effects of lifestyle change. Our analysis indicated that

common CVD medications did not have significant effects on peripheral blood gene expression and suggest that alterations in individual genes and multigene pathways were attributable to lifestyle changes.

We showed that intensive lifestyle modification can significantly alter the expression of numerous genes associated with leukocyte function, vascular inflammation, and lipid homeostasis. Fold-changes we observed during a 1-year period in patients undergoing lifestyle modification were comparable in magnitude to differences in expression reported for patients with CVD compared with healthy controls.8,10 Similar to traditional risk factors, however, these molecular changes seem dynamic, and persistence over time may depend on longterm adherence to healthy behaviors. The number of significantly altered genes increased >5-fold from week 12 to week 52, suggesting that patients who maintain healthy lifestyle behaviors for longer periods of time are likely to experience more diverse molecular change than patients participating in short-term activities. In addition, some conventional risk factors and gene expression profiles showed regression toward baseline after 12 weeks, which corresponded with a lower percentage of participants meeting compliance targets, particularly for exercise and stress management (Table VIII in the Data Supplement). Adherence to cardiovascular treatment regimens involving lifestyle change is particularly difficult, and many patients usually adhere only partially to programmatic goals.48 Thus, personal motivation and strict adherence are key factors for successful long-term cardiovascular benefit.

Limitations

Intensive lifestyle programs for CVD risk reduction involve demanding behavioral changes that require motivation and a significant time commitment, which likely restrict the applicability of such programs to patients in general. Accordingly, it was impractical to use a randomized study design, which may limit the conclusions that can be drawn from the data, although well-designed case-control studies may be similar to randomized trials for estimating treatment effects.49 We analyzed the data using a per-protocol (on-treatment) approach but included all patients who completed the program regardless of whether they strictly adhered to the program guidelines. The multifaceted nature of the program precluded us from precisely defining the relative contribution of each component in driving molecular and physiological changes; however, the correlation analysis indicated that many observed changes in gene expression may be attributable to weight loss and physical activity. Furthermore, we could not evaluate long-term changes in gene expression and CVD risk factors beyond 1 year, and we could not assess whether the observed results are achievable outside a controlled clinical environment.

During the intervention, our patients remained under the care of their primary physicians, who may have prescribed medications other than cardiovascular medications. We conducted a subgroup analysis to account for potential effects of common cardiovascular medications on patterns of gene expression, but it is possible that other medications not examined in these analyses influence leukocyte gene transcription.

Peripheral blood is a complex tissue with diverse cell populations whose relative abundance is dynamic over time. Gene expression studies using whole blood cannot distinguish the effects of cellular demographics from signatures of physiological response. To address this issue, we examined published expression signatures of major leukocyte populations to infer specific cell types involved in response to lifestyle modification; however, rare cell types not examined may play an important role in CVD risk reduction.

Conclusions

CVD prevention through intensive lifestyle changes leads to improvements in clinically relevant cardiac risk factors that may be important in the pathogenesis of atherosclerosis.⁵⁰ However, the extent and significance of molecular changes that accompany CVD risk reduction during lifestyle change are poorly understood. There is growing evidence that peripheral blood gene expression reflects the pathophysiology of circulating leukocytes and the vascular endothelium. An increased understanding of dynamic changes in the leukocyte transcriptome during lifestyle modification thus may be crucial for evaluating the efficacy of risk-reduction strategies and understanding mechanisms by which diet and exercise affect cellular processes involved in CVD risk reduction. Conventional risk factors such as low-density lipoprotein cholesterol and blood pressure continue to be primary targets of clinical management for patients with CVD, but as new biochemical and genomic risk factors are identified, it is becoming clear that measures of vascular health go beyond traditional risk factors. A key finding of this study is that successful, sustained modulation and dramatic downregulation of genes, including LTF, through healthy changes in lifestyle may have positive effects on vascular health not readily apparent from traditional risk factors. Future studies are needed to validate changes in gene expression during lifestyle modification and examine the effect of healthy behaviors on leukocyte function and leukocyte-endothelium interactions that are important for cardiovascular health.

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Disclosures

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CLINICAL PERSPECTIVE

Lifestyle interventions designed to reverse or stabilize progression of coronary artery disease successfully ameliorate clinically relevant risk factors important in the pathogenesis of atherosclerosis, but little is known about molecular alterations that accompany lifestyle changes. This study examined the effect of a rigorous cardiovascular risk-reduction program on peripheral blood gene expression profiles to characterize molecular responses and identify regulatory pathways important to cardiovascular health. During intensive lifestyle modification, expression of numerous individual genes and multigene pathways associated with leukocyte function, vascular inflammation, and lipid homeostasis were significantly downregulated. Similar to traditional risk factors, however, changes in the leukocyte transcriptome were dynamic, and persistence over time may depend on long-term adherence to healthy behaviors. As growing evidence suggests that peripheral blood gene expression reflects the pathophysiology of circulating leukocytes and health of the vascular endothelium, successful and sustained modulation of gene expression through changes in lifestyle may have beneficial effects on the vascular system of cardiac patients not apparent from traditional risk factors. Monitoring gene expression is, therefore, potentially useful for determining the vascular benefits of clinical interventions and may identify important targets for drug development.

ORIGINAL ARTICLE

Fatigued on Venus, sleepy on Mars—gender and racial differences in symptoms of sleep apnea

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Abstract

Objective Clinical guidelines for the care of obstructive sleep apnea (OSA) recommend evaluation of daytime sleepiness but do not specify evaluation of fatigue. We studied how subjects with and without OSA experience fatigue and sleepiness, examining the role of gender and race.

Design, setting, patients Consecutive subjects entering our heart health registry completed validated questionnaires including Berlin Questionnaire for OSA, Fatigue Scale, and Epworth Sleepiness Scale. Data analysis was performed only with Whites and Blacks as there were too few subjects of other races for comparison.

Results Of 384 consecutive subjects, including 218 women (57 %), there were 230 Whites (60 %) and 154 Blacks (40 %), with average age of 55.9 ± 12.8 years. Berlin Questionnaires identified 221 subjects (58 %) as having high likelihood for OSA. Fatigue was much more common in women (75 %) than in men (46 %) with OSA (p<0.001), while frequency of fatigue was similar in women (30 %) and men (29 %) without OSA (p=0.86). In multivariate analysis, men with OSA were sleepier than women; Black men with OSA had higher

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Epworth scores (mean±SD, 12.8±5.2) compared to White men (10.6±5.3), White women (10.0±4.5), and Black women (10.5±5.2), p=0.05. These gender differences were not related to the effects of age, body mass index, perceived stress, sleep duration, or thyroid function.

Conclusions Women report fatigue more commonly with OSA than men. Men experience sleepiness more commonly with OSA than women. The findings suggest that evaluation of sleep disorders must include an assessment of fatigue in addition to sleepiness to capture the experience of women.

Keywords Sleepiness · Fatigue · Obstructive sleep apnea syndrome · Sleep apnea

Abbreviations

BMI	Body mass index
CMS	Centers for Medicare and Medicaid Services
CPAP	Continuous positive airway pressure
EDS	Excessive daytime somnolence
ESS	Epworth sleepiness scale
ICHP	Integrative Cardiac Health Project
IRB	Institutional Review Board
OSA	Obstructive sleep apnea
OSAS	Obstructive sleep apnea syndrome
PSS	Perceived stress scale
SD	Standard deviation
TSH	Thyroid-stimulating hormone

Introduction

Obstructive sleep apnea (OSA) is an important disorder because of its high prevalence [1], the constellation of comorbidities associated with the disorder [2], and the substantial symptoms that OSA may cause [3]. OSA is labeled obstructive sleep apnea syndrome (OSAS) when adequate numbers of apneas and hypopneas are accompanied by symptoms such as excessive daytime sleepiness (EDS), fatigue, inattentiveness, moodiness, or morning headaches [4].

In addition to their role in diagnosis of the syndrome, symptoms also serve as important indicators to track response to therapy. A recently published clinical guideline for evaluation and management of OSA [5] endorses the evaluation of sleepiness with the Epworth Sleepiness Scale (ESS) [6] but does not suggest an assessment of fatigue. Other recently published research demonstrates that the ESS is commonly used to evaluate OSA-associated symptoms without incorporation of a scale to measure fatigue [7, 8]. However, subjects with OSA more frequently use terms such as fatigue, tiredness, or lack of energy rather than sleepiness to characterize their symptoms pointing to a lack of connection between the questions asked to elicit symptoms and the experience of symptoms by patients with OSA [9, 10].

Furthermore, symptoms of OSAS are not experienced to the same degree by patients with similar severities of OSA as measured by apnea-hypopnea index or oxygen desaturation [9, 11]. The range and severity of symptoms caused by the sleep disruption of OSA appear to be trait-like qualities for an individual patient [12, 13] and differ markedly among individuals [11]. Substantial data support the contention that sleepiness and fatigue are independent manifestations of sleep disorders and that patients may report one or the other, both or neither while carrying the same objective diagnosis of OSA [9, 10, 14, 15]. While prior research has examined gender differences in symptoms of OSAS [9, 15], we sought to broaden our understanding of the experience of sleepiness and fatigue in subjects with and without OSA with special attention to the roles of gender and race. Such an evaluation has not been previously undertaken.

Methods

This study was conducted in accordance with the amended Declaration of Helsinki and with the approval of the Institutional Review Board (IRB) at the Walter Reed National Military Medical Center in Bethesda, Maryland, which granted approval for the protocol designated #372910. The study design is an analysis of data prospectively collected on consecutive patients enrolled in the Integrative Cardiac Health Project (ICHP) Registry. The ICHP Registry is a cardiovascular disease prevention program operating in a research Center of Excellence for the United States Department of Defense. Because the Registry database could be deidentified before data analysis, an exempt protocol was approved by the IRB (#20012) to perform a secondary analysis on the Registry data and patient consent was not required for the purpose of this analysis. Patients are self-referred or referred to the ICHP Registry by a health care provider to improve habits of diet, exercise, sleep, and stress management. ICHP is accessible to military health care beneficiaries including active duty service members, retirees, and civilian dependents. The program therefore enrolls a broad spectrum of subjects including a variety of races and ethnic backgrounds, both genders, and a range of ages from 18 to 90 years. The typical patient entering the program is found to have two to four risk factors for cardiovascular disease.

Upon entry, subjects are asked to complete a series of questionnaires (described in detail below) to gather information on demographics, current symptoms, and lifestyle habits. Among the questionnaires are validated surveys to assess sleep behaviors, sleep quality, and daytime symptoms. Data from the questionnaires are reviewed during a medical interview with a nurse practitioner who performs a physical examination with anthropomorphic measures. Patients also submit blood for laboratory tests including a thyroid function panel.

Berlin questionnaire

Of questionnaires available to screen patients for sleep apnea, the Berlin Questionnaire is one of the most commonly utilized and best validated [16]. Permission was granted by the copyright owner to use the questionnaire for this study. As measured by the questionnaire, patients with persistent and frequent signs and symptoms are considered to be at high risk for sleep apnea. Questions about symptoms demonstrated internal consistency (Cronbach correlations, 0.86 to 0.92). With a positive Berlin questionnaire, sleep apnea was predicted with a sensitivity of 0.86, a specificity of 0.77, a positive predictive value of 0.89, and a likelihood ratio of 3.79.

Fatigue Scale

The Fatigue Scale is borrowed from the Stanford Patient Education Research Center [17]. The Stanford web site stipulates that the scale is free to use without permission. The Fatigue Scale asks subjects to express their experience of fatigue from 0 to 10 for the previous 2-week period. The Fatigue Scale was tested on 122 subjects deriving a data set with mean score of 4.89 ± 2.71 points. Subjects who circle 5 to 6 express mild fatigue, 7 to 8 moderate fatigue, and 9 to 10 severe fatigue.

Epworth sleepiness scale

The ESS is the most widely used tool to estimate the subjective symptom of daytime sleepiness [18]. Dr. Johns permits use of the ESS by individual people (including clinicians and researchers) free of charge. Subjects are asked to use a scale of 0 to 3 to estimate their likelihood of dozing in eight different

situations in recent weeks. The individual scores are summed and possible scores range from 0 to 24. Sleepy subjects score 11 or higher and sleepiness can be categorized by scores: 11 to 14, mild sleepiness; 15 to 19, moderate sleepiness; and 20 to 24, severe sleepiness.

Perceived stress scale

The perceived stress scale (PSS) is one of the most widely accepted measures of stress [19]. Dr. Cohen's web site, where a copy of the PSS is provided, states that permission for use of the scale is not necessary when use is for academic research or educational purposes. This validated 14-item questionnaire asks the subject how often certain experiences of stress occurred in the last month and is designed to measure the degree to which situations in one's life are appraised as stressful. With item responses from 0 to 4, the range of possible scores is 0 to 56 with higher scores correlating with higher stress. The PSS is designed for use in community samples with at least a junior high school education. The items are easy to understand and the response alternatives are simple to grasp. Moreover, the questions are quite general in nature and hence relatively free of content specific to any subpopulation group. Score in the low 20s reveal moderate stress levels while scores approaching 30 are substantial and concerning.

Statistical analysis

Continuous data that were normally distributed (as determined by the Shapiro–Wilk test) are presented using means with standard deviations (mean \pm SD): Univariate comparisons are made using the two-sample *t* test or analysis of variance. Categorical data are presented as counts with proportions and groups are compared using Fisher's exact test. Sleepiness was defined as a score on the ESS of 11 or higher, and fatigue was defined as a score on the Fatigue Scale of 5 or higher.

To adjust for confounding variables, multivariable linear regression was used with either the Fatigue Scale or ESS as the dependent variable and independent variables to include gender, race, age, body mass index (BMI), PSS, thyroid-stimulating hormone (TSH), and sleep duration. Separate models were examined for subjects with and without OSA. Independent variables that were significant in univariate analysis at the p<0.25 level were entered into the multivariable models [20]. Data were analyzed using IBM SPSS Statistics for Windows (v. 21.0. IBM Corp. Armonk, NY).

Results

12.8 years consistent with a spectrum of lifestyles from actively working to semi-retired to fully retired adults. Of the 446 consecutive subjects, 249 women (56 %), there were 234 Whites, 155 Blacks, 13 Hispanics, 2 Asians, and 42 others. Because there were so few participants represented by racial categories other than Whites and Blacks, the other races were not considered further, leaving 389 subjects. Five subjects did not have Epworth or Fatigue Scale data leaving 384 evaluable subjects with an average age of 55.9 ± 12.8 years and including 218 women (57 %).

Fatigue was found in 181 subjects (48 %) and sleepiness in 160 subjects (42 %). The proportion of subjects reporting neither fatigue nor sleepiness, fatigue only, sleepiness only, or both fatigue and sleepiness are shown in Table 1 by race and gender. Women had higher Fatigue Scale scores (Table 2, p=0.02), and complained more frequently of fatigue (115 of 215, 53 %) than men (66 of 165, 40 %), while men had significantly higher Epworth scores (Table 3, p=0.02), and complained more frequently of sleepiness (77 of 166, 46 %) compared to women (83 of 218, 38 %).

Berlin Questionnaires identified 219 subjects (58 %) as having high likelihood for OSA. There was no difference in thyroid function between subjects with and without a positive Berlin score (mean±SD in each group was 2.2 ± 1.4 , p=0.61). Symptoms of fatigue and sleepiness are presented in Figs. 1 and 2. Fatigue associated with OSA is more commonly experienced by women than by men, p<0.001 (Table 2 and Fig. 1). Sleepiness in association with OSA is more frequently experienced by men, particularly Black men, than by all other categories, p=0.05 (Table 3 and Fig. 2).

Univariate analysis of Fatigue Scale scores (Table 2) demonstrates significantly higher scores in younger age groups (p<0.001), and in subjects with positive Berlin score (p<0.001), higher perceived stress scores (p<0.001), and shorter sleep duration (p<0.001). Notably, Fatigue Scale scores were not different according to TSH, nor were they different according to BMI categories after factoring in presence of OSA (Table 2).

Univariate analysis of ESS scores (Table 3) show higher scores in younger age categories (p<0.001), and in subjects with positive Berlin scores (p<0.001), higher perceived stress scores (p<0.001), and shorter sleep duration (p<0.001). ESS scores were not different according to TSH, nor were they different according to BMI categories after factoring in presence of OSA (Table 3).

To control for confounding demographic and clinical characteristics, multivariable linear regression was used to examine both fatigue and sleepiness. With the Fatigue Scale score as the dependent variable, age and perceived stress score both significantly correlated with fatigue in subjects without OSA. Younger age and higher stress were associated with more fatigue. However, among subjects with OSA, gender was also

Subject descriptors	All subjects ^a ($n=380$)	Black women ($n=89$)	White women $(n=126)$	Black men ($n=63$)	White men ($n=102$)	p value
Age (years)	56.0±12.8	52.9±12.0	56.9±12.0	52.1±13.6	59.9±12.9	< 0.001
BMI (kg/m ²)	30.7±5.4	32.5±5.8	29.2±5.3	31.2±4.6	30.7±5.1	< 0.001
Not fatigued, not sleepy Fatigued only	141 (37 %) 81 (21 %)	23 (26 %) 28 (31 %)	54 (43 %) 29 (23 %)	25 (40 %) 6 (9 %)	39 (38 %) 18 (18 %)	0.007
Sleepy only	58 (15 %)	9 (10 %)	14 (11 %)	15 (24 %)	20 (20 %)	
Both fatigued and sleepy	100 (26 %)	29 (33 %)	29 (23 %)	17 (27 %)	25 (24 %)	
Fatigued only Sleepy only Both fatigued and sleepy	81 (21 %) 58 (15 %) 100 (26 %)	28 (31 %) 9 (10 %) 29 (33 %)	29 (23 %) 14 (11 %) 29 (23 %)	6 (9 %) 15 (24 %) 17 (27 %)	18 (18 %) 20 (20 %) 25 (24 %)	

 Table 1
 Symptoms by gender and race

Age, BMI, and the proportion of subjects reporting neither fatigue nor sleepiness, fatigue only, sleepiness only, or both fatigue and sleepiness are shown by race and gender. For age and BMI, comparisons between groups are made using analysis of variance. For the categorical variables of fatigue and sleepiness, comparisons between groups are made using Fisher's exact test. Fatigue was defined as a score on the Fatigue Scale of 5 or higher, and sleepiness was defined as a score on the Epworth Sleepiness Scale of 11 or higher

^a Three hundred eighty of the 384 subjects had both Epworth and fatigue data

significantly associated with fatigue, with women reporting higher fatigue scores compared to men (Table 4).

Multiple linear regression using ESS score as the dependent variable showed that the independent variable of sleep duration was significantly associated with sleepiness among subjects without OSA, with longer sleep times associated with lower ESS scores. However, among subjects with OSA, PSS and gender were significantly associated with ESS scores. Increases in perceived stress were associated with higher levels of sleepiness. Since female gender was the reference group in the model, the positive beta coefficient for gender indicates a greater degree of sleepiness in men compared to women (Table 5).

Table 2 Fatigue scale data compared for subjects with and without OSA

Fatigue scale		Total	Total			No OSA			OSA		
		n	mean±SD	p value	n	mean±SD	p value	n	mean±SD	p value	
All subjects		380	4.4±2.4		161	3.4±2.2		219	5.1±2.3		
Gender	Females Males	215 165	4.7±2.5 4.1±2.3	0.022	105 56	3.5±2.3 3.3±2.1	0.58	110 109	5.8±2.2 4.5±2.3	< 0.001	
Race	Black White	152 228	4.8±2.4 4.2±2.4	0.028	56 105	3.6±2.3 3.4±2.1	0.54	96 123	5.4±2.3 4.9±2.4	0.1	
Gender × race	Black females White females	89 126	5.3±2.5 4.2±2.4	0.002	33 72	4.0±2.4 3.3±2.1	0.26	56 54	6.0±2.3 5.5±2.2	< 0.001	
	Black males	63	4.0±2.1		23	$3.0{\pm}1.9$		40	4.6±2.0		
	White males	102	4.1 ± 2.4		33	3.6 ± 2.2		69	4.4 ± 2.4		
Age (years)	<50 50-59	106 131	5.6±2.0 4.5±2.5	< 0.001	39 48	4.6±2.0 3.6±2.3	< 0.001	67 83	6.2±1.8 5.0±2.5	< 0.001	
	60+	143	3.5±2.2		74	2.8±1.9		69	4.3±2.3		
BMI	Normal Overweight	51 129	4.4±2.7 4.0±2.4	0.02	31 78	3.5±2.5 3.3±2.2	0.61	20 51	5.8±2.6 5.0±2.5	0.47	
	Obese	200	4.7±2.3		52	3.6 ± 2.1		148	4.3±2.3		
Berlin questionnaire	Normal OSA	161 219	3.4±2.2 5.1±2.4	< 0.001	161	3.4±2.2		219	5.1±2.4		
TSH (mU/L)	<4.5 4.5 +	361 19	4.4±2.4 5.0±2.2	0.29	154 7	3.4±2.2 4.3±1.6	0.3	207 12	5.1±2.4 5.4±2.4	0.68	
PSS (of 56 points)	<21 21+	176 200	3.4±2.3 5.3±2.2	< 0.001	92 69	2.7±2.0 4.4±2.1	< 0.001	84 131	4.1±2.4 5.8±2.1	< 0.001	
Sleep duration (h)	<6 6+	120 257	5.4±2.3 4.0±2.4	< 0.001	37 122	4.3±2.5 3.2±2.1	0.005	83 135	5.8±2.1 4.7±2.4	< 0.001	

Fatigue scale data are presented according to various categories listed on the left column of the table. Comparisons between groups are made using the two-sample *t* test or analysis of variance

Table 3	Epworth	score data	a compared	l for sub	jects with	and y	vithout	OSA

Epworth score		Total			No OS	SA		OSA		
		n	mean±SD	p value	n	mean±SD	p value	n	mean±SD	p value
All subjects		384	9.4±5.2		163	7.5±4.7		221	10.9±5.1	
Gender	Females Males	218 166	8.9±5.0 10.1±5.3	0.024	106 57	7.4±4.8 7.5±4.4	0.87	112 109	10.3±4.9 11.4±5.3	0.096
Race	Black White	154 230	10.4±5.4 8.7±4.9	0.002	57 106	8.7±5.1 6.8±4.3	0.015	97 124	11.5±5.3 10.4±4.9	0.11
Gender \times race	Black females White females	91 127	9.9±5.2 8.2±4.8	0.001	34 72	8.9±5.0 6.7±4.6	0.11	57 55	10.5±5.2 10.0±4.5	0.05
	Black males	63	11.2±5.6		23	8.4±5.4		40	12.8±5.2	
	White males	103	9.4±5.1		34	7.0 ± 3.5		69	10.6 ± 5.3	
Age (years)	<50 50–59	108 133	11.2±5.5 9.3±4.9	< 0.001	41 48	8.8±5.3 7.8±4.3	0.038	67 85	12.7 ± 5.1 10.1 ± 5.0	0.002
	60+	143	8.2±4.8		74	6.5±4.3		69	10.0 ± 4.8	
BMI (kg/m ²)	Normal Overweight	51 131	8.7±5.7 8.8±5.4	0.056	31 79	6.2±4.7 7.3±4.8	0.09	20 52	12.6±5.1 11.0±5.5	0.26
	Obese	202	10.0 ± 4.9		53	8.5±4.4		149	10.6±4.9	
Berlin questionnaire	Normal OSA	163 221	7.5±4.7 10.9±5.1	< 0.001	163	7.5±4.7		221	10.9±5.1	
TSH (mU/L)	<4.5 4.5 +	365 19	9.3±5.2 10.9±4.3	0.19	156 7	7.3±4.7 10.3±4.3	0.1	209 12	10.8±5.2 11.3±4.4	0.74
PSS (of 56 points)	<21 21+	177 203	8.2±4.7 10.4±5.3	< 0.001	93 70	7.3±4.6 7.7±4.7	0.55	84 133	9.1±4.7 11.8±5.1	< 0.001
Sleep duration (h)	<6 6+	121 260	11.0±5.5 8.7±4.9	< 0.001	37 124	9.2±5.5 6.9±4.3	0.023	84 136	11.7±5.3 10.3±4.9	0.051

Epworth Sleepiness Scale data are presented according to various categories listed on the left column of the table. Comparisons between groups are made using the two-sample *t* test or analysis of variance

Discussion

The salient findings of this study are that symptoms of sleepiness and fatigue experienced in association with OSA have different frequencies by gender and by race even after controlling for confounding variables such as age, BMI, thyroid





Fig. 1 Frequency of fatigue by race and gender. Fatigue associated with obstructive sleep apnea (OSA) is more commonly experienced by women than by men, p < 0.001



Fig. 2 Frequency of sleepiness by race and gender. Sleepiness in association with obstructive sleep apnea (OSA) is more frequently experienced by men, particularly Black men, than by all other categories, p=0.05

Table 4	Results of	of multivariate	linear regression	for fatigue score
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Independent variables	No OSA		OSA Adjusted coefficients							
	Adjusted coefficients									
	Beta (95 % CI)	<i>p</i> value	Beta (95 % CI)	<i>p</i> value						
Age	-0.04 (-0.07 to -0.02)	<0.001	-0.03 (-0.05 to -0.004)	0.022						
BMI	NS		NS							
PSS	0.09 (0.05 to 0.13)	< 0.001	0.09 (0.05 to 0.12)	< 0.001						
Sleep duration	-0.21 (-0.45 to 0.03)	0.079	-0.14 (-0.36 to 0.09)	0.23						
TSH	NS		NS							
Gender ^a	NS		-1.02 (-1.59 to 0.45)	0.001						
Race ^b	NS		-0.11 (-0.72 to 0.50)	0.72						

To adjust for confounding variables, multivariate linear regression was used with Fatigue Scale as the dependent variable and independent variables to include gender, race, age, BMI, PSS, TSH, and sleep duration. Separate models were examined for subjects with and without OSA. Independent variables that were significant in univariate analysis at the p < 0.25 level were entered into the multivariate models. NS indicates that a variable was not significant in univariate analysis and was therefore not included in the multivariate model

BMI body mass index, OSA obstructive sleep apnea, PSS perceived stress scale, TSH thyroid-stimulating hormone

^a Females are reference group

^b Blacks are reference group

questionnaire designed to quantify sleepiness will not suffice. Likewise, sleepiness cannot be properly evaluated with a questionnaire aimed at the symptom of fatigue. It is of major interest that a sizable proportion of the study subjects (10 to 31 % according to gender and race) experienced fatigue without sleepiness.

The proper documentation of symptoms is also important to gain appropriate allowance by insurance carriers. The National Coverage Determination for continuous positive airway pressure (CPAP) therapy published by the Centers for Medicare and Medicaid Services (CMS) sets the standard for Medicare coverage and is adopted by other insurance providers [21]. CMS considers CPAP therapy reasonable and necessary for patients with a mild category of OSA (apnea hypopnea index or respiratory disturbance index greater than or equal to five events and less than or equal to 14 events per hour) if appropriate symptoms are documented [21]. Without symptoms properly documented in these patients with a mild index of severity, their CPAP therapy would not be justifiable to insurance carriers, including CMS.

Table 5 Results of multivariate linear regression for Epworth sleepiness score

Independent variables	No OSA		OSA							
	Adjusted coefficients		Adjusted coefficients							
	Beta (95 % CI)	<i>p</i> value	Beta (95 % CI)	p value						
Age	-0.04 (-0.09 to 0.01)	0.15	-0.03 (-0.09 to 0.03)	0.28						
BMI	0.10 (-0.06 to 0.26)	0.20	NS							
PSS	NS		0.17 (0.08 to 0.25)	< 0.001						
Sleep duration	-0.71 (-1.27 to -0.16)	0.012	-0.19 (-0.71 to 0.33)	0.47						
TSH	0.31 (-0.22 to 0.84)	0.25	NS							
Gender ^a	NS		1.59 (0.27 to 2.90)	0.018						
Race ^b	-1.30 (-2.89 to 0.29)	0.11	-0.97 (-2.37 to 0.43)	0.17						

To adjust for confounding variables, multivariate linear regression was used with Epworth Sleepiness Scale as the dependent variable and independent variables to include gender, race, age, BMI, PSS, TSH, and sleep duration. Separate models were examined for subjects with and without OSA. Independent variables that were significant in univariate analysis at the p<0.25 level were entered into the multivariate models. NS indicates that a variable was not significant in univariate analysis and was therefore not included in the multivariate model

BMI body mass index, OSA obstructive sleep apnea, PSS perceived stress scale, TSH thyroid-stimulating hormone

^a Females are reference group

^b Blacks are reference group

The finding of increased sleepiness and fatigue with shorter sleep duration conforms to prior studies that have demonstrated a strong correlation of acute and chronic sleep deprivation with decreased alertness, impaired psychomotor vigilance testing, and shorter sleep latency on mean sleep latency test [22–24]. Likewise, the observation that sleepiness and fatigue decrease with higher age groups agrees with prior research [25, 34]. We speculate that this finding of diminished symptoms with age is further explained by the circumstances that retirement and semi-retirement in older age groups allows for more opportunities to sleep and to sleep on a self-determined schedule.

The association of higher stress levels with increased symptoms of fatigue and sleepiness deserves to be addressed with further scrutiny. Potential explanations are that higher perceived stress levels intensify the experience of other symptoms such as fatigue and sleepiness. It is equally plausible that high stress levels negatively affect sleep latency, sleep continuity, and the restorative quality of sleep. These theoretical considerations warrant further study and suggest that successful stress management may be an intervention as valuable as expansion of sleep time for symptom management.

The findings of a differential experience of symptoms from disturbed sleep according to gender and race are not unique to this study. Recent reports include the observations that women more frequently experience sleep-onset insomnia than men [26] and that White women are more likely to report use of a sleep aid (prescription or nonprescription) [27]. Periodic limb movements of sleep and associated symptoms are much more common in Whites compared to Blacks [28], while estimated prevalence of narcolepsy and its symptoms are higher in women than men and in Blacks than in other racial groups [29]. Blacks are more likely to experience sleep phase advance [30] and both Blacks and women are more likely to report extremes of sleep duration (less than 5 h or greater than 9 h) [31, 32] with attendant elevation in C-reactive protein [33].

In a published review of gender differences, Ye and colleagues raise the concern that differences in symptoms on presentation with OSA may lead to the under-recognition of sleep pathology in women [15]. They note that while the Sleep Heart Health Study [34] did not find the frequency or severity of sleepiness to be affected by gender, the Wisconsin Sleep Cohort Study [1] did report a higher proportion of women with daytime sleepiness than men. Data from the Sleep Heart Health Study analyzed for impact of ethnicity but not gender [35] did find less subjective sleepiness among Blacks than Whites. Other studies report that men tend to report more sleepiness than women [36], and that women prefer to describe their subjective experience of sleep-disordered breathing using terms to denote fatigue, tiredness, and lack of energy [9, 18]. One explanation for these disparate findings regarding the different experiences of symptoms is that the questionnaire instruments may not have allowed participants, especially women, the chance to register symptoms of fatigue.

Research into the differential experience of the subjective symptoms of sleepiness versus fatigue is acknowledged to be difficult [37] and a variety of potential explanations for the disparate published reports above have been advanced. Among the explanations are that men have a less accurate perception of their pathologies than do women, that cultural influences make men less willing to acknowledge symptoms, or that there may be a gender-based neurophysiological explanation for the different experience of OSA [9]. Explanations of racial differences include the impact of socioeconomic conditions [8, 38] and varied subjective interpretation of symptoms due to differing life experiences [39]. However, there are studies that demonstrate clear anatomical differences of the upper airway according to gender and race [40]. Furthermore, a gene association study [41] and gene segregation analysis [42] have documented associations of sleep apnea vulnerability according to race.

A limitation of the current study is that subjects were categorized for the presence of sleep apnea using the Berlin Questionnaire rather than polysomnography. The Berlin Questionnaire is a reasonably sensitive and specific clinical screening tool but it is not the gold standard, suggesting that an appropriate follow-on study may be to repeat our measures in a large population with polysomnography. Another limitation is that races other than Whites and Blacks were not represented in sufficient numbers to include them in this analysis. The symptoms experienced by men and women of other races deserve further discovery.

Another factor potentially limits the ability to generalize our findings to other populations. A third of the subjects in our study sample reported fewer than 6 h of sleep per night. This degree of sleep restriction is higher than that reported in civilian populations and may be a reflection of the military culture from which our study sample derives [43]. A survey of the average sleep duration in the USA reported in 2009 that approximately 40 % of military personnel obtained less than 5 h of sleep per night compared with 8 % in the general population [43].

The data from the current study indicate that the subjective symptoms of sleepiness and fatigue are experienced not just according to gender or race but differentially by both factors simultaneously. These findings underscore the clear need to evaluate patients presenting with sleep disorders using instruments that measure more than just sleepiness and incorporate measures of fatigue and other descriptors commonly voiced by patients suffering from sleep conditions. Clinical centers evaluating patients for sleep disorders would be well advised to incorporate validated instruments for assessing symptoms of fatigue in addition to sleepiness. Future clinical guidelines should incorporate the recommendation that the evaluation of patients with sleep complaints include assessment of symptoms such as fatigue. Acknowledgments The Integrative Cardiac Health Project (ICHP) Registry group consists of the listed authors (see cover page) and the following individuals who have contributed to the work presented in this manuscript but not meeting requirements for authorship: Elaine Walizer RN, MSN, study coordinator; Marion Jones, CRNP, MSN, nurse practitioner; Meghan Rooney, CRNP, MSN, nurse practitioner; Ellen Turner MS, exercise physiologist and health coach; Nancy Tschiltz RD, dietitian; Joy Halsey, RD, dietitian; Marilyn Grunewald, stress management specialist. This study received funding from The Henry M. Jackson Foundation for the Advancement of Military Medicine.

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A Systematic Approach Incorporating Family History Improves Identification of Cardiovascular Disease Risk

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Background: Although family history (FH) is an independent predictor of cardiovascular disease (CVD) risk, traditional risk scores do not incorporate FH. Nurse practitioners routinely solicit FH but have no mechanism to incorporate the information into risk estimation. Underestimation of risk leaves clinicians misinformed and patients vulnerable to the CVD epidemic. Objective: We examined a systematic approach incorporating FH in CVD risk assessment, validating risk reclassification using carotid intima-media thickness (CIMT), a surrogate measure of atherosclerosis. Methods: Of 413 consecutive patients prospectively enrolled in the Integrative Cardiac Health Project Registry, a subgroup of 239 was low or intermediate risk by the Framingham Risk Score. A systematic approach for the assessment of FH was applied to this subgroup of the registry. A positive FH for premature CVD, defined as a first-degree relative having a CVD event before the age of 55 years in men and 65 years in women, conferred reclassification to high risk. Reclassification was validated with CIMT results. Results: Chart audits revealed adherence to the systematic approach for FH assessment in 100% of cases. This systematic approach identified 115 of 239 (48%) patients as high risk because of positive FH. Of the reclassified patients, 75% had evidence of subclinical atherosclerosis by CIMT versus 55% in the patients not reclassified, P < 0.001. Logistic regression identified positive FH for premature CVD (odds ratio, 2.6; P = 0.001) among all variables, as the most significant predictor of abnormal CIMT, thus increasing risk for CVD. Conclusions: The Integrative Cardiac Health Project systematic approach incorporating FH into risk stratification enhances CVD risk assessment by identifying previously unrecognized high-risk patients, reduces variability in practice, and appropriately targets more stringent therapeutic goals for prevention.

KEY WORDS: cardiovascular disease, family history, primary prevention, risk assessment

Cardiovascular disease (CVD) is the leading cause of death and disability in the United States and Europe.^{1,2} On the basis of numerous analyses performed

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to determine the thresholds for increased risk, family history (FH) of premature CVD is defined as a first-degree relative having a CVD event before the age of 55 years in men and 65 years in women.^{3–12} With this definition, FH of premature CVD is an independent and robust predictor of risk. When FH is positive, individual risk for CVD is increased by as much as 5-fold.¹⁰ Although US and European guidelines include positive FH as a high-risk factor, traditional risk scoring systems do not. Nurse practitioners routinely inquire about FH in clinical practice, but there is variability in the approach to capture and interpret the data.^{5,13,14}

The Framingham Risk Score (FRS), the most widely used CVD risk assessment tool, significantly underestimates risk because it does not incorporate FH data.^{15,16} Studies show FRS to be only 50% accurate in identifying patients at high risk for heart disease.¹⁵ In fact, up to 75% of patients experiencing an acute coronary syndrome are assessed as low risk by the FRS.¹⁷ When FH is not used in risk assessment, a large subgroup of the population at risk for CVD remains unrecognized, leaving them unaware of their threatened health status. Failing

to identify these high-risk individuals precludes clinicians from prescribing targeted and risk-specific self-care interventions aimed at CVD prevention.¹³

Although FH has been repeatedly demonstrated to be a high risk factor of CVD, current guidelines provide no mechanism for the systematic collection, interpretation, and risk score adjustment using this information. We implemented a systematic approach for the assessment of FH to standardize identification of high-risk patients and used carotid intima-media thickness (CIMT) to validate the high-risk reclassification.^{18,19}

Methods

This investigation was conducted with the approval of the institutional review board at Walter Reed National Military Medical Center in Bethesda, Maryland. The study design is a subgroup analysis of data prospectively collected on consecutive patients enrolled in the Integrative Cardiac Health Project (ICHP) Registry. The ICHP Registry is a CVD prevention program operating in a research Center of Excellence for the US Department of Defense. All subjects gave informed consent for participation in the registry, and the study was conducted according to the principles stated in the Declaration of Helsinki.

The ICHP offers military healthcare beneficiaries a 6-month tailored CVD risk reduction program. Patients who join the program by self or provider referral must be adults older than 17 years. All patients seen at the ICHP are categorized upon baseline assessment as low, intermediate, or high risk for CVD by the FRS. In addition, ICHP patients receive results of a detailed CVD risk assessment and a personalized preventive health plan. As part of the ICHP Registry, patients receive a CIMT, which is maintained as a long-term CVD outcome measure. The CIMT findings are not used to calculate the patient's CVD risk status. The following variables were collected on all patients who attended the ICHP from 2008 to 2011: age, gender, ethnicity, FRS, FH status, CIMT and diagnoses of CVD, hypertension, dyslipidemia, and diabetes.

Upon entry to the ICHP, patients undergo a cardiovascular-focused history and physical examination. Medical history, including smoking history, is elicited with a written question as part of a questionnaire, and the responses are verified verbally by a nurse practitioner at the time of the physical examination. medical history such as hypertension, diabetes, and dyslipidemia is also elicited on the questionnaire, validated verbally by a nurse practitioner and reconciled with data recorded in the patient's medical record. Body mass index (BMI) is calculated with the formula kilograms divided by the square of height in meters using measured height and weight from a medical-grade weight scale and stadiometer. Blood pressure is first measured after the patient has been sitting quietly for 5 minutes using a

GE DINAMAP PRO Series 100–400V2. Five minutes later, a second blood pressure reading is taken, and the 2 values are averaged for the record. All cardiovascular-relevant laboratory data are obtained in the blood chemistry laboratory at the medical facility, with the laboratory certified by the Clinical Laboratory Improvement Amendments.

At a subsequent appointment, the patients were informed of their CVD risk status and were provided therapeutic goals specific to their determined risk category. Although the patients in all risk categories (low, intermediate, and high) received recommendations for healthy behavior change, the high-risk patients were targeted with aggressive treatment goals for cholesterol, blood pressure, and weight management.

This analysis was limited to a subgroup of ICHP patients whose calculated FRS showed low or intermediate 10-year risk because the high-risk patients could not be reclassified to a higher level of risk. Diabetes is considered by the FRS to be a high-risk factor, and therefore, any patient with diabetes was excluded from this analysis.

Risk Assessment (Carotid Intima-Media Thickness)

The CIMT findings were reviewed and evaluated by 1 sonographer oriented to the purposes of the project but blinded to the FH information for each patient. Images were obtained on a single ultrasound machine (SonoSite MicroMaxx 3.4.3; Bothell, Washington) using a linear array 5- to 10-MHz transducer with standardized image settings, including resolution mode, depth of field, gain, and transmit focus. All sonograms were obtained with the patients supine with the head facing the contralateral side. Electrocardiograms were recorded simultaneously. The sonographer, also trained in the measurement of CIMT, performed the analyses with commercially available software (Sonocalc IMT, Bothell, Washington). Carotid intima-media thickness was determined from images of the far wall of the distal common carotid arteries (immediately proximal to the carotid bulb) and reported as the mean value for the bilateral measurement. The near (intimal-luminal interface) and far (medial-adventitial interface) field arterial wall borders were manually traced for measurement of mean CIMT (millimeters) across a 10-mm arterial segment. A mean CIMT measurement of greater than the 75th percentile cutoff value, based on age and gender, in at least 1 carotid vessel was defined as an abnormal CIMT, as proposed by the American Society of Echocardiography Carotid Intima-Media Thickness Task Force.²⁰ This cutoff value has been used in a prior large atherosclerosis outcomes study, the Arterial Biology for the Investigation of the Treatment Effects of Reducing Cholesterol (ARBITER) Study, with CIMT as its main outcome measure.²¹

Impact Assessment

For CVD risk assessment, ICHP nurse practitioners evaluated FRS and FH status. The FRS, which takes into account age, gender, smoking, systolic blood pressure, total cholesterol, and high-density cholesterol levels, was determined using a web-based tool.²² A systematic approach to evaluating FH was applied to standardize risk stratification beyond the FRS (see Figure). The ICHP nurse practitioners were trained using a standardized operating procedure (SOP) detailing the collection of FH during the initial assessment of each patient. This SOP defined positive FH of premature CVD as a first-degree relative (parent or sibling) having a CVD event before the age of 55 years in men and 65 years in women.^{11,12} Cardiovascular disease events included myocardial infarction; cardiovascular revascularization; and diagnosis of coronary disease, stroke, or transient ischemic attack. The family tree was explored in detail for these CVD events, specifically in first-degree relatives and for the age of occurrence. Any first-degree family member meeting these criteria conferred a high-risk designation irrespective of the FRS result. Patients who were unable to provide FH (for example, patients who are adopted and do not have FH information) were excluded from the analysis. Chart audits were performed on 100% of cases to verify adherence to the systematic approach outlined in the SOP.

Analyses were performed using the Statistical Package for the Social Sciences (version 20.0).²³ Descriptive and frequency statistics were presented as mean (SD) or percentage. Student *t* test for continuous variables and χ^2 analysis for categorical variables were used. Logistic regression was performed to assess the predictive impact of factors on the likelihood of a patient having an abnormal CIMT.

Results

Of 413 patients, 19 patients (4.6%) were excluded for lack of FH data, leaving 394 for this analysis. Using the FRS, 239 of 394 patients (61%) were classified as low or intermediate risk. Frequency and descriptive analyses revealed a normally distributed population by age with no missing data. Demographic findings showed a mean age of 49 years (range, 20–76); 59% were women; 51%, white; 25%, black; 6%, Hispanic; and 1%, Asian, with 17% undeclared or other. The mean body mass index was 30.5 kg/m². The population was characterized by hypertension (40%), dyslipidemia (71%), and smoking (2%).

Chart audits revealed adherence to the systematic approach for FH assessment in 100% of the 239 patients who were in the low or intermediate FRS category. The systematic approach identified 115 of 239 patients (48%) as having positive FH for CVD. Table 1 displays the comparison between the 2 groups (positive FH and negative



FIGURE. The Integrative Cardiac Health Project systematic approach incorporating family history in CVD assessment.

TABLE 1 Baseline Characteristics of Population at Low and Intermediate Cardiovascular Disease Risk												
N = 239	Negative FH, n = 125	Positive FH, n = 114	Р									
Age, y	44.9 (12.18)	54.3 (10.16)	0.02 ^a									
Gender (female)	55%	64%	0.17									
BMI, kg/m ²	29.5	31.3	0.39									
Active smoker	3%	2%	0.86									
Hypertension	31%	39%	0.18									
Dyslipidemia	74%	70%	0.47									
FRS	3.01 (3.21)	4.5 (4.19)	0.001 ^a									
Glucose, mg/dL	89.8 (10.1)	92.8 (9.68)	0.84									
CIMT (abnormal)	55%	75%	<0.001 ^a									

Data are presented as mean (SD) or percentage. t test is used for continuous variables. χ^2 analysis is used for categorical variables. P values are given for the comparison between FH groups.

^aDenotes statistical significance.

FH). Between FH groups, age, FRS, and CIMT were different. The patients with a positive FH were older (54.3 vs 44.9 years, P = 0.02). The mean FRS scores were statistically different (positive FH, 4.5; negative FH, 3.0; P < 0.001), although this difference is not clinically important because both scores indicate low risk. In validating the reclassification using CIMT, the proportion of patients with an abnormal CIMT was clinically and statistically different between groups, with a higher percentage in the positive FH group (75% vs 55%, P < 0.001). No effect of confounding was detected because there was no difference between groups using χ^2 analysis for gender, BMI, smoking history, hypertension, and dyslipidemia.

Logistic regression was performed to assess the impact of factors on the likelihood that patients would have an abnormal CIMT (Table 2). The model contained 5 independent variables (race, gender, FH category, diagnoses of hypertension and dyslipidemia). Age was not included in the model because age is one of the normative factors used as a cutoff value in the definition of normal versus abnormal CIMT.²⁰ The full model containing all predictors was statistically significant, χ^2 (11, n = 239) = 41.1, *P* < 0.001, indicating that the model was able to distinguish between normal and abnormal CIMT. The model as a whole explains between 16% and 22% of the variance in CIMT status and correctly classified 69% of cases after inclusion of the predictors. Two of the independent variables made a unique statistically significant contribution to the model (black race: odds ratio [OR], 5.8; P = 0.02; 95% confidence interval [CI], 1.3–26.9, and presence of positive FH: OR, 2.4; P = 0.006; 95% CI, 1.3–4.5). In an effort to find the most parsimonious model predicting abnormal CIMT,²⁴ logistic regression was repeated using the 2 contributing variables, black race and presence of positive FH. This new model containing the 2 predictors was statistically significant, χ^2 (6, n = 239) = 28.6, *P* < 0.001, indicating that the model was able to distinguish between normal and abnormal CIMT. The model as a whole explains between 11% and 16% of the variance in CIMT status and correctly classified 69% of cases after inclusion of the predictors. Although black race was no longer a significant predictor in the new model, presence of positive FH remained the only significant predictor contributing to the logistic regression model (black race: OR, 0.528; *P* = 0.290; 95% CI, 0.162–1.725, and presence of positive FH: OR, 2.64; P = 0.001; 95% CI, 1.47–4.73). The Hosmer-Lemeshow test showed goodness of fit with a significance of 0.86.

Discussion

Although national guidelines recognize the importance of FH for CVD risk, these guidelines provide no mechanism to instruct practitioners on how to translate this FH information to a more accurate determination of risk for the individual patient.^{1,2,5} In fact, there has been

							95% C	l for OR
Predictors of Abnormal CIMT	В	SE	Wald	df	Р	OR	Lower	Upper
Black race	1.761	0.781	5.088	1	0.024 ^a	5.816	1.260	26.856
Gender	0.441	0.318	1.921	1	0.166	1.554	0.833	2.897
FH positive	0.883	0.318	7.691	1	0.006 ^a	2.418	1.296	4.513
Diagnosis of hypertension	0.540	0.346	2.435	1	0.119	1.716	0.871	3.382
Diagnosis of dyslipidemia	0.196	0.347	0.320	1	0.572	1.217	0.616	2.404
Constant	-1.736	0.808	4.612	1	0.032	0.176		

TABLE 2 Logistic Regression Model

The model contained 5 independent variables (race, gender, positive FH, diagnosis of hypertension, and diagnosis of dyslipidemia). The full model containing all predictors was statistically significant, χ^2 (11, n = 239) = 41.1, P < 0.001, indicating that the model was able to distinguish between normal and abnormal CIMT.

^aDenotes statistical significance.

a call for evidence on the value of systematically using FH in CVD risk assessment.⁵

Investigation of FH requires a systematic approach in which there is minimized variability in assessment of risk among clinicians because there are numerous criteria needed to fulfill the definition of positive FH. These criteria are complex and require an in-depth review of the family tree including gender, relationship to the patient, and age of onset of CVD. A simple yes/no question is inadequate to provide the relevant data to illicit an accurate FH for risk estimation.⁵

Our study population of mostly overweight, latemiddle-aged subjects with a variety of races is fairly typical of a population seeking medical evaluation for CVD risk estimation. One risk factor that makes our sample population stand out as different from the US population is the very low prevalence of self-reported smoking behavior (2%), which is substantially lower than US norms (19%).²⁵ A potential explanation for this discrepancy is that there have been initiatives for health promotion that champion smoking cessation, including a ban of smoking on site in the medical facility. Furthermore, self-referred patients seeking wellness in a CVD risk reduction program may also be less likely to smoke.

We have shown that, among asymptomatic, previously low- or intermediate-risk patients by FRS, the use of a systematic approach for the incorporation of FH resulted in identifying a substantial proportion of patients at high risk for CVD. These patients would have otherwise been told that they were not at high risk for CVD. In addition, we have demonstrated the feasibility of implementing a systematic approach for incorporating FH, an easily accessible and inexpensive data point.²⁶

The validity of this reclassification was substantiated using CIMT in the positive FH group to find 75% abnormal CIMT results compared with 55% abnormality in the group with negative FH. This is consistent with findings from the Framingham Offspring Study, a large population-based cohort of families in which CVD events were validated prospectively in both parents and offspring.¹¹ On the basis of that study, an association was found between parental history and subclinical atherosclerosis among offspring measured by CIMT.

Our study highlights the predictive value of including FH in assessment of risk for CVD. By logistic regression, positive FH was shown to be a robust predictor, indicating that patients with presence of positive FH were more than twice as likely to have an abnormal CIMT compared with those with negative FH, when controlling for all other factors in our data set. Although positive FH was an independent predictor, other factors including age, race, gender, and diagnoses of hypertension and dyslipidemia were not predictors of an abnormal CIMT. This may be explained by an underlying atherosclerotic mechanism causing functional abnormalities in offspring of patients with premature CVD, independent of known vascular risk factors.^{27–29}

The mean age of the patients with a positive FH was greater than of the patients with negative FH in our cohort. This finding may be explained by the fact that older study subjects will have older siblings who are more likely to have experienced a cardiovascular event and younger study subjects will more likely have younger siblings who have not yet developed CVD. The older sibling's event gives the older study subject a positive FH, whereas younger study subjects are more likely to have a negative FH.

The lack of a mechanism to incorporate FH in CVD risk assessment is a major gap in current practice. This article suggests a systematic approach to translate the evidence for FH into clinical practice. When patients at high risk for CVD are properly identified, they are given appropriate therapeutic goals to match their heightened risk category, and more attention is paid to healthy lifestyle behavior change. Ultimately, incorporating FH in risk assessment is a way to personalize preventive therapies aimed at combating the epidemic of CVD.

Limitations

Limitations include the use of CIMT as a surrogate measure for CVD events. However, this is a commonly used strategy to overcome expense, feasibility issues, and risk associated with radiological studies such as electron beam computerized tomography and computed tomographic angiography.¹⁸

Although our sample population shows some characteristics that mirror the US population generally such as overweight,³⁰ an important characteristic that deviates from the US population is the very low prevalence of smoking status (2%). This difference may limit our ability to generalize our findings to the population at large. Another potential limitation may be referral bias because patients with positive FH may have a heightened sense of concern regarding their CVD health before entering the program.

Furthermore, data collection did not include all individual variables thought to influence CVD, although variables necessary for FRS calculation were captured. A further limitation is that approximately 5% of our patients were unable to provide FH.

Conclusions

Translation of evidence into practice is dynamic, and mechanisms to help clinicians accomplish translation continue to evolve. Recent evidence indicates that positive FH has predictive validity.⁴ This study demonstrates that a reproducible systematic approach for adding FH to current practice enhances predictive value and identifies high-risk patients who, at present, are not captured.

This report describes a mechanism that addresses a current gap in clinical practice. The findings of this report are sufficiently promising to warrant further implementation and validation in other settings, using different study designs and outcome measures.

What's New and Important

- Family history for premature CVD, defined as a first-degree relative having a CVD event before the age of 55 years in men and 65 years in women, confers a high-risk classification for CVD as validated by a surrogate marker of atherosclerosis.
- A systematic approach for incorporation of FH for premature CVD will enhance the identification of high-risk patients.
- Incorporating FH in risk assessment is a way to personalize preventive therapies aimed at combating the epidemic of CVD.

We urge practitioners to adopt a systematic approach to incorporate FH in CVD risk assessment to provide patients with more accurate risk stratification and to target preventive interventions for high-risk individuals. We believe that implementation of such a systematic approach would have a global impact on patients at risk for CVD.

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Appendix B Gantt Charts

D	0	Task Name	Start	Finish	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
1		Task #1: BATTLE trial - CLOSED	Thu 9/1/05	Sun 3/29/15	6	:	:		:	:	:	:	:		\Rightarrow
2		Presentations and manuscripts	Wed 9/1/10	Sun 3/29/15]					6				-	Þ
3															
4	\checkmark	Task #2: CADRe 5-Yr Follow-up - CLOSED	Wed 3/1/06	Mon 9/29/14			:			-	-			<u> </u>	
5	\checkmark	IRB protocol approval	Tue 5/23/06	Tue 5/23/06		• 5	/23								
6	\checkmark	Participant enrollment/Data collection	Fri 2/2/07	Wed 6/30/10						-					
7	\checkmark	Data reconciliation	Fri 10/1/10	Fri 9/30/11						(-				
8	\checkmark	Conduct analysis	Wed 12/1/10	Thu 1/31/13									Þ		
9	\checkmark	Publication plan	Wed 12/1/10	Fri 2/15/13]								Þ		
10		Presentations and manuscripts	Tue 2/1/11	Sun 3/29/15											Þ

ID	0	Task Name	Start	Finish	2
1		Task #3: Continue CPP	Thu 9/1/05	Sun 9/29/19	
2		Enrollment/Data collection	Thu 9/1/05	Sun 9/29/19	
3		Advance data modeling	Fri 1/1/10	Sun 9/29/19	
4		Outreach	Fri 1/1/10	Sun 9/29/19	
5		Ultra personal empowering	Mon 1/2/12	Sun 9/29/19	
6		Outcomes analysis	Mon 1/1/07	Sun 9/29/19	
7		Target subgroup popns	Fri 12/1/06	Sun 9/29/19	
8		Presentations/manuscripts	Mon 4/2/07	Sun 9/29/19	
9		Upgrade database	Fri 10/1/10	Wed 12/31/14	
10					
11	\checkmark	#3.1: Validate CV risk	Tue 12/5/06	Mon 9/29/14	
12	\checkmark	IRB protocol approval	Tue 12/5/06	Tue 12/5/06	
13	\checkmark	Continuing review approved	Wed 10/7/09	Wed 10/7/09	
14		Data collection	Mon 1/1/07	Sun 3/29/15	
15		Conduct analysis	Wed 8/1/07	Tue 9/29/15	
16		Presentations/manuscripts	Mon 3/2/09	Tue 9/29/15	



D	0	Task Name	Start	Finish	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
1		Subtask #3.2: Initiate ZENITH trial	Fri 1/1/10	Sun 9/29/19)		:	:	:		:	:	:	:		
2	\checkmark	Protocol development	Fri 1/1/10	Wed 5/9/12	2			-								
3	\checkmark	Protocol approval WRNMMC/MRMC	Thu 5/10/12	Mon 6/10/13												
4	\checkmark	Protocol approval at WMC/MRMC	Fri 5/17/13	Wed 7/31/13					۲							
6	\checkmark	Study execution planning	Fri 6/14/13	Wed 4/30/14												
7		Recruitment/enrollment/data collection	Tue 7/15/14	Fri 9/28/18	:					•						
8		Conduct analysis	Wed 4/1/15	Sun 9/29/19								:	:	:		
9		Biomolecular studies	Tue 7/15/14	Sun 9/29/19						•	-					
10		Publication plan	Fri 1/2/15	Sun 3/29/15							0					
11]											
12		Subtask #3.3: CPP Prospective Registry	Thu 9/1/11	Sun 9/29/19			6	:			:	:	:	:		
13	\checkmark	Protocol development/submission	Thu 9/1/11	Fri 3/30/12			6	-								
14	\checkmark	Protocol approvals (WRNMMC/MRMC)	Mon 4/2/12	Wed 11/13/13					-							
15		Recruitment/enrollment/data collection	Mon 11/3/14	Sun 9/29/19							Ċ	:	:	:		
16		Data reconciliation/analysis	Fri 1/2/15	Sun 9/29/19)							:	:	:		
17		Manuscript preparation	Mon 2/2/15	Sun 9/29/19									:	:		

ID	0	Task Name	Start	Finish	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
1	\checkmark	Subtask #3.4: CV Risk in Tramatic Amputations	Thu 3/1/12	Mon 9/29/14	ł												
2	\checkmark	Protocol approval	Fri 8/10/12	Fri 8/10/12	2				•	8/10							
3		Recruitment/enrollment/data collection	Thu 3/1/12	Sun 9/29/19)					:		:	:	:	:		
4	\checkmark	Protocol modification for genomics/analytes	Thu 8/1/13	Thu 1/2/14	ł												
5		Data analysis	Mon 9/3/12	Sun 9/29/19)				6	:		:	:	:	:		
6		Presentations and manuscripts	Tue 1/1/13	Sun 9/29/19)							1	1				
7																	
8		Task #4: Global Profiling/CRC Completion	Thu 10/1/09	Sun 3/29/15	5	6	1	1	1	1	<u> </u>	Þ					
9		Followup data analysis/publication	Thu 10/1/09	Sun 3/29/15	5			1	1	1		Þ					
10	\checkmark	Enroll program participants	Wed 2/25/09	Wed 2/25/09)	2/2	5										
11	\checkmark	Manuscript on gene expression	Thu 10/1/09	Thu 10/31/13	6		:	:	:	:							
12	\checkmark	TaqMan SNP analysis	Thu 4/14/11	Fri 5/30/14	ŀ												
13	\checkmark	Metabolite profiling analysis	Thu 4/14/11	Tue 12/31/13	6				1	1						- - - - - - - - - - - - - - - - - - -	
14		Assimilation of PET/CT data	Thu 3/1/12	Sun 3/29/15	5					1		Þ					
15		Conduct molecular analysis	Wed 9/15/10	Sun 3/29/15	5		6	1	1	1		Þ					
16		Presentations & publications	Thu 4/14/11	Sun 3/29/15	5				1	1		Þ					
17																	
18	\checkmark	Task #6: Natural History of Pre-Diabetes	Mon 8/2/10	Mon 9/29/14	ŀ			1	1	1							
19	\checkmark	Protocol development/submission	Thu 3/1/12	Mon 5/7/12	2				۲							- - - - - - - - - - - - - - - - - - -	
20	\checkmark	Protocol approval at WRNMMC/MRMC	Thu 5/10/12	Tue 6/4/13	6												
21	\checkmark	Protocol approval at WMC/MRMC	Fri 5/17/13	Wed 7/24/13	6					۲						- - - - - - - - - - - - - - - - - - -	
22		Study execution and planning	Mon 9/1/14	Wed 12/31/14	ŀ						6)					
23		Recruitment/enrollment/data collection	Thu 1/1/15	Mon 12/31/18	8								1	-	1		

ID	0	Task Name	Start	Finish	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
1		Task #7: Morbid Obesity	Fri 1/13/06	Sun 3/29/15				:	:	:	:	:	:		\Rightarrow
2	\checkmark	Protocol approved at WMC	Fri 1/13/06	Fri 1/13/06	•	1/1	3								
3	\checkmark	Protocol approved at TATRC	Fri 6/15/12	Fri 6/15/12								• (6/15		
4	\checkmark	Enroll patients	Mon 7/24/06	Fri 8/30/13				:	:	:					
5	\checkmark	Obtain blood and tissue samples	Mon 7/24/06	Mon 3/31/14			:	:	:	:	:	:	:		
6		Conduct molecular analysis	Mon 10/1/12	Sun 3/29/15								(-	Þ
7		Presentations and manuscripts	Tue 1/1/13	Sun 3/29/15											Þ
8															
9		Task #8: Global Long-term	Fri 8/17/12	Sun 3/29/15								6	:		Þ
10	\checkmark	Protocol approved at WMC	Fri 8/17/12	Fri 8/17/12								•	8/17		
11	\checkmark	Protocol approved at TATRC	Thu 5/2/13	Thu 5/2/13									♦ 5	12	
12	\checkmark	Enroll patients	Sat 6/1/13	Tue 4/1/14											
13	\checkmark	Obtain blood samples and data	Sat 6/1/13	Tue 4/1/14											
14		Conduct molecular analysis	Tue 10/1/13	Sun 3/29/15									(Þ
15		Presentations and manuscripts	Wed 1/1/14	Sun 3/29/15											Þ